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CONTENTS

SPECIAL ARTICLE		DENTAL SECTION (Cont'd)
Stripped Bladder Relines Itself MEDICAL ARTICLES	1	The Incipient Carious Lesion 10 Severe Reactions to Unintentional Intravascular Injections of Penicillin 10
Cystic Fibrosis With Fecal Retention (Meconium Ileus Equivalent) The Use of Potassium in the Treatment of Heart Disease	4 5	Personnel and Professional Notes1' PREVENTIVE MEDICINE Occurrence of Cholera in Iran1'
Isolation of the Trachoma Agent in Cell Culture FROM THE NOTE BOOK	9	Malaria 1 Anemia Secondary to Penicillin Treatment 1 Coccidioidomycosis Outbreak in Canoga Park,
Paralytic Poliomyelitis-1964	12 12 12 12 13 13	Calif. 1 Botulism on Queen Charlotte Islands 2 Air Pollution is a Costly Luxury 2 Milker's Nodules 2 New Type of Accident 2 Air Pollution Linked to Excess Deaths in New York 2
Naval Medical Research Reports Lab Inspection & Accreditation Mycoplasma DENTAL SECTION	14 14 14	Acid Stream Pollution Found Heavy in Appalachia 2 Rat Tapeworm Infection in Man 2 Know Your World 2 EDITORIAL DESK
Naval Dental Research Reports Stannous Fluoride in Naval Personnel Geographic Distribution of Caries-Resistant Naval	15 15	Operational Medicine Refresher Series 2 Career Development Program 2 14th Annual Seminar on Ob-Gyn 2 In Memoriam 2

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ceptible to use by any officer as a substitute for any item or article in its original form. All readers of the News Letter are urged to obtain the original of those items of particular interest to the individual.

Change of Address

Please forward changes of address for the News Letter to: Commanding Officer, U.S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland 20014, giving full name, rank, corps, and old and new addresses.

FRONT COVER: U.S. NAVAL HOSPITAL, PENSACOLA, FLORIDA. The present Naval Hospital is the fifth of a series of hospitals reaching back to the early years of the 19th Century. Florida was ceded to the United States in 1821, and soon thereafter the Pensacola Navy Yard was established. Surgeon Isaac Hulse was assigned duty at Pensacola on 14 November 1826 and spent most of his shore duty at that station being in charge of the hospital at intervals until his death in 1856. This hospital was probably of Spanish origin.

Congress, on 10 July 1832, appropriated \$30,000 for construction of a hospital at Pensacola. A two-story brick building was built in 1833 to 1835 on a low bluff facing Pensacola Bay near old Fort Barrancas about three-fourths of a mile to the west of the Navy Yard. In 1836 a twelve-foot brick wall was built around the hospital at a cost of \$11,921.25.

The neglected and dilapidated buildings of the third Naval Hospital were torn down in 1917 and one story frame buildings were erected on the same site providing accommodations for 142 patients. This hospital served the naval air activities during World War I and the post-war years. In 1938, incident to the great expansion of activities at the Naval Air Station, reconstruction and modernization of the hospital was authorized with WPA and PWA funds. The original hospital reservation of 15 acres within the brick wall was increased to 40.46 acres by transfer to the hospital of land on the north and west of the compound to the boundary line of Fort Barraneas.

Ceremonies dedicating the new hospital building were held on 15 February 1941. During 1942 and 1943, the hospital capacity was expanded by the construction of a row of four H-type, single story wooden ward buildings and one pavilion ward at the northwest corner of the reservation. These wards were connected with the hospital by a long ramp.

The issuance of this publication approved by the Secretary of the Navy on 4 May 1964.

SPECIAL ARTICLE

STRIPPED BLADDER RELINES ITSELF

Medical World News 6(29): 33-35, August 6, 1965.

A Washington, D. C., urologist has successfully treated recurring multifocal cancer of the bladder by removing the bladder lining. Dr. Roger Baker, chief of urology at Georgetown University Medical Center, who developed the technique, says that the lining regenerates to its normal state within three months after excision. The cancer lesions apparently do not recur in the new lining.

Dr. Baker's findings indicate that his technique may offer an important replacement for radical surgery in treating serious urinary tract lesions. He has already achieved regeneration of an entire human bladder and, in addition, has perfected a method that may soon be employed clinically to regenerate the entire human ureter.

Until now, excision of each lesion via a transurethral approach has been the standard treatment for multifocal bladder cancer. But this technique controls the cancer only temporarily and lesions usually recur within several months. Most often, the patient must eventually undergo cystectomy.

Urologists have been reluctant to attempt removal of the lining to eliminate the cancer lesions because of the possibility of fibrous tissue forming on the bladder's muscle wall. This would prevent regeneration of the lining and cause severe contracture of the organ.

Further, many experts believe that affected patients have either a genetic or acquired predisposition to tumor formation in the bladder lining. But Dr. Baker finds no data to support the theory. If it were true, he says, patients who have cancer of the pelvis of one kidney would develop cancer in the other "in a statistically high percentage of cases."

The observation that they do not leads him to believe that the disease is not genetically controlled and that removal of the entire mucous membrane of the bladder, before the disease invades the muscularis, could inhibit the lesions and eliminate the need for eventual cystectomy. Dr. Baker experimented with his technique in dogs for many years before applying it clinically. He now has three patients who have undergone successful removal of the epithelial lining of the bladder for treatment of multifocal cancers.

One patient, followed up for 32 months, has not had a recurrence of the disease. The same patient had suffered recurrences every few months when the standard transurethral technique was used to remove the individual lesions.

The patient, a 48-year-old engineer, was first seen in 1959, when he underwent nephroureterectomy for a "huge transitional cell cancer of the renal pelvis." During the next 28 months, he was cystoscoped eight times. Each time. Dr. Baker removed several grade II transitional cell carcinomas from the bladder and urethra.

In November 1962, Dr. Baker removed the entire bladder lining, hoping to stop the cancer once and for all. He approached the bladder suprapubically, opening it wide, and injecting a saline solution under pressure between the lining and the bladder wall, to separate the mucosa for excision. He carried the excision deep into the superficial muscle to ensure total mucosal resection, repeating this process until all that remained was a narrow disk of lining, two millimeters wide, around the ureteral orifice. Then he chemically cauterized the urethra with 50% phenol for 30 seconds, and irrigated it with alcohol and saline.

The surgeon then inserted an empty quarter-inch Penrose drain into the bladder, closed the organ in two layers with chromic catgut, brought the end of the drain through the wound, and sutured it to the skin. Finally, he inserted an indwelling urethral catheter with a 5-cc bag, which the patient wore for four weeks. The bladder drain remained in place until bleeding was no longer a problem.

Postoperatively, the patient experienced some stress incontinence, slight dysuria, and, after the catheter was removed, terminal urinary dribbling. However, these symptoms diminished rapidly. He was discharged 30 days later, maintaining full urinary control, voiding maximum volumes of 100 cc every one to two hours, and experiencing no discomfort.

The patient had been working full time with no urinary complaints when he came back to the hospital for a five-month follow-up examination. He was voiding about every two hours during the day and three to four times at night, with volumes ranging from 150 cc to 200 cc. "There was no discomfort with bladder fullness, no urgency, no problem with urinary control, and no discomfort in voiding," says Dr. Baker. Maximum bladder capacity was 225 cc, and there was no urethral stricture.

The bladder lining had regenerated, the Washington surgeon reports. It was paler than normal, and the cell layers varied in thickness from one to four and five cells, but they showed no mucosal lesions. However, Dr. Baker found a single papillary lesion in the urethra at the peno-scrotal junction, which was diagnosed as transitional cell carcinoma, grade I, and was removed.

Endoscopy performed 11 months postoperatively again revealed no recurrence of bladder lesions and no recurrence of the urethral lesion. The bladder mucosa now appeared normal.

At the 31-month follow-up examination, Dr. Baker again found a normal bladder lining and no recurrence of lesions. But he did find another transitional cell carcinoma in the urethra, leading him to conclude that urethral cauterization does not appear to be effective. "In this case," he says, "either the phenol was not in the urethra long enough or was not of high enough concentration, or perhaps the technique just doesn't work at all!"

After the lining was removed, Dr. Baker was especially concerned about fibrosis and contracture of the bladder. At the five-month follow-up, he found no extensive fibrosis, although the regenerated bladder epithelium showed some thickening, edema, and inflammation. "This observation deserves specific attention," he points out, "as it has generally been assumed that loss of a major area of the epithelial lining of the bladder, and certainly its total loss, would result in contracture with gross reduction in capacity."

Besides using the regeneration phenomenon in treating multifocal bladder cancers that have not invaded the muscularis of the bladder, Dr. Baker has used it to grow entire new bladders after cystectomy. Although he has successfully used the technique in

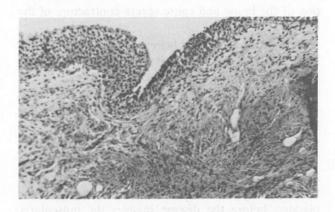
more than 20 patients since 1959, he finds that it "is not yet practical from a clinical standpoint." The process takes four months, during which time the patient must wear a collection bag on his abdomen. Most patients, he notes, refuse to become even temporary "social cripples."

He now prefers to provide a substitute bladder from the patient's own body, usually a segment of large or small bowel, which provides almost immediate urinary function. But Dr. Baker has not given up on bladder regeneration: He is now trying different methods of accelerating the process.

The ureter is also amenable to regeneration, he maintains. He has successfully regenerated entire ureters in dogs, and is planning to try the technique in adults and children who have massive dilatation of the ureter. The procedure consists of removing the diseased portion of ureter and connecting the two severed ends with a thin strip of ureter tissue.

The Washington urologist declares: "We have proved that the entire ureter will regenerate, from the kidney all the way down to the bladder. Other conditions treatable by regeneration, he believes, are strictures at the ureteropelvic junction and perhaps even hypospadias.

Dr. Baker reports two current theories on regeneration of the bladder and bladder lining. Some investigators say that it results from a migration of epithelial and muscle cells from the mucous membrane and muscularis of the lower ureter. Others, himself included, hold that totipotent mesenchymal sheath cells themselves will develop into the two cell types-epithelia and muscle.



Regenerated epithelium has a pale appearance, but tissue is normal in other respects.

In the case of bladder lining, he says, the new growth doesn't spread out from a single point, but develops in patchwork fashion all over the muscularis. "Cell migration may play a role, but it is only a minor one."

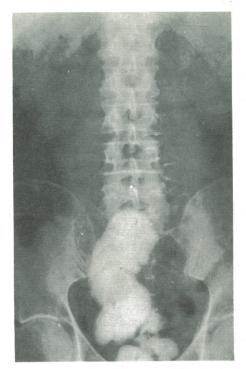


Ureter cross-section shows regrowth of both muscularis and mucous membrance after patching with strip of tissue.

Regeneration depends on several factors, Dr. Baker maintains. To begin with, "an inductor" must be present to stimulate the process. These inductors are present throughout the body. For example, in a cut hand, "something yet unknown develops in the wound to induce fibrous tissue to heal the defect; something else then stops the healing process, or the scar would grow to the size of a house." Urine must be present as the inductor in the bladder he says. "If a bladder is removed and the ureters are left down in the pelvis but the urine is diverted from the site, no new bladder forms."

Organ regeneration occurs best when the organ is left in its normal position in the body, Dr. Baker reports. "It is easy to regenerate a bladder in the pelvis of the dog, but if the ureters are both brought beneath the abdominal wall to one side of the dog, only normal bladder mucous membrane regenerates, not muscle."

Dr. Baker and his colleagues, Dr. William C. Maxted and Ned DiPasquale, are planning to gain further control over the regeneration phenomenon.



Bowel section forms new "bladder" after cystectomy, in another Baker procedure.

They expect to study the effects of infection and certain hormones on the process. They already know that the process is accelerated by adrenal extract, pituitary extract, testosterone, vitamins A and C, and use of the organ during regeneration.

The Washington researchers will also examine limitations of the process. "We know that brain, lung, and kidney will not regenerate." But in dog experiments, they have been able to achieve regeneration of 50% of the circumference of the large segments of the large bowel. This may have eventual clinical application for patients undergoing abdominal perineal resection for cancer. Dr. Baker remarks that "patients could regenerate a normal bowel and not have to be restricted to use of a colostomy for life."

Few investigators are today working on regeneration, Dr. Baker notes, but as research in this area progresses, he predicts that techniques to promote regeneration will take their place alongside organ transplantation, organ substitution, and installation of artificial organs to prolong normal life.

MEDICAL ARTICLES

CYSTIC FIBROSIS WITH FECAL RETENTION (MECONIUM ILEUS EQUIVALENT): REPORT OF TWO CASES

Robert M. Sigler MD, Resident in Surgery, Henry H. Reeves MD, Resident in Pediatrics, Hugh B. Lynn MD, Section of Pediatric Surgery, Edmund C. Burke MD, Section of Pediatrics. Mayo Clin Proc 40(6): 477–480, June 1965.

Cystic fibrosis (also referred to as fibrocystic disease of the pancreas) with its sometimes attendant neonatal meconium ileus is a well-recognized entity.1 The disease is characterized by deficiency or lack of pancreatic intestinal enzymes and by abnormal mucoprotein in the small intestine, increased viscosity of endobronchial secretions, and increased concentration of sodium chloride in the sweat. In some 10 to 20% of these patients, intestinal obstruction (meconium ileus) occurs in the neonatal period, due to inspissated, tenacious, putty-like meconium that requires surgical removal. Fecal retention as a later complication has been recognized less frequently and there have been few case reports. Herein we report two cases, one of which responded to nonoperative management.

Report of Cases

Case 1. A girl, almost 6 years old, first was seen at the Mayo Clinic in January 1958 with the chief complaint of a mass in the right lower quadrant of her abdomen; it had been noted during routine physical examination when she was 1½ years old. This mass had been noted again when she was 3½ but no symptoms were referable at that time to the gastrointestinal tract. Six months later, a barium enema demonstrated a filling defect in the cecum and at exploratory laparotomy a noninflamed enlarged appendix filled with "hard putty-like material" was removed. Examination of the remainder of the large and small bowel failed to reveal further abnormality. Six months postoperatively, abdominal pain developed and again a mass in the right lower quadrant was noted. The mass subsequently varied in size and often disappeared after bowel movements which were described as being foul.

When seen here, 1½ years postoperatively, she had a chronic cough, and a roentgenogram of her thorax was compatible with fibrocystic disease. Physical examination revealed a mass in the right lower quadrant, clubbing of the fingers, and protuberant abdomen. The concentration of chloride in the sweat was 97 mEq per liter (normal, 50 mEq), a value which established the diagnosis of fibrocystic disease.

case of bladder lining he says, the new

The patient was treated with pancreatin (Viokase) and a low-fat diet, and there was improvement in the odor and consistency of the stool. On follow-up examination in 1962, an asymptomatic mass was noted in the right lower quadrant and presumably represented fecal material in the region of the cecum.

Infection of the upper part of the respiratory tract was not a problem in this patient at the time an abdominal mass first was noted. It was only later that a history of chronic cough and foul stools was obtained. It is interesting that the diagnosis of cystic fibrosis was not evident at laparotomy.

Case 2. A 14-year-old boy was seen at the Mayo Clinic in July 1964 with intestinal obstruction. He reported that low abdominal pain and obstipation had started 4 days prior to admission and were unrelieved by enemas and intravenous administration of fluids by his home physician. He had had frequent infections of the upper part of the respiratory tract since the age of 3 months and bulky foul stools since the age of 3 years. The diagnosis of fibrocystic disease had been confirmed when he was 6½ years old, at which time the thoracic roentgenogram was typical and the sweat chloride concentration was 108 mEq per liter. His condition immediately prior to his present illness had been satisfactory; he had been

having two bowel movements daily on a regimen of five tablets of pancrelipase (Cotazym) daily.

Findings on physical examination included distended abdomen, high-pitched tinkling bowel sounds, and peristalsis of the intestines visible through the abdominal wall. There was a large smooth mass in the right lower quadrant. Proctoscopic examination, plain roentgenogram of the abdomen, and barium enema localized the mass to the cecal and lower ilial region. There were multiple distended loops of small bowel above the obstruction.

Treatment consisted of intravenous administration of fluids, placement of a Miller-Abbott tube, and multiple cleansing enemas. After decompression of the upper part of the bowel for a few hours, 5 ml of mucolytic agent (N-acetyl-L-cysteine) was injected through the Miller-Abbott tube at 4-hour intervals for three doses. The patient began to pass copious quantities of putty-like stool with dramatic relief of pain and distension. He was dismissed on the fourth hospital day and was urged to take at least five tablets of pancrelipase daily and to restrict himself to a low-fat diet.

Comment

Neonatal meconium retention that produces mechanical obstruction is well known. A similar syndrome in older children is being reported with increasing frequency. Snyder and co-workers 2 recently reviewed the literature and found 19 cases, including their 3, of "meconium ileus equivalent." 3 All but three of these had required surgical intervention. Etiologic factors which have been suggested include diet change, failure to take or outgrowing the dosage of prescribed enzymes, and dehydration from any cause.

It seems reasonable that, if this entity were recognized as a cause of intestinal obstruction, appropriate medical therapy might preclude the need for operation. However, one should be alert to detect intussusception which may occur.4 In cases in which there is no obstruction, the mass may be indistinguishable from a neoplasm on barium studies.5

A plain roentgenogram of the abdomen will be very helpful in diagnosis of mechanical obstruction, and barium enema often will localize the lesion to the cecum or terminal part of the ileum. Fibrocystic disease, past or present, should alert one to the possibility of retained feces.

In view of the success in case 2, it would seem appropriate to institute vigorous nonoperative treatment to relieve the obstruction in "meconium ileus equivalent," This should include rehydration, decompression of the proximal part of the bowel with a long intestinal tube (which will also allow instillation of pancreatic enzymes, or mucolytic agents, or both), and enemas. If operation is required, the classic findings are a terminal ileum, cecum, appendix, and, sometimes, right colon filled with putty-like material which may be removed through enteric stomas; resections may be necessary if attempts at removal of the material fail.

Summary

We have presented two cases of late complications of cystic fibrosis due to fecal retention. In one case, the diagnosis of cystic fibrosis was not evident until after operation had been performed for an asymptomatic abdominal mass in the right lower quadrant. In the other case which presented as intestinal obstruction, operation was avoided because the entity of "meconium ileus equivalent" was recognized.

References

- Lynn, H. B.: Meconium Ileus. Am Surgeon 30: 597-601, September 1964.

- 1964.
 Snyder, W. H. Jr., Gwinn, J. L. Landing, B. H., and Asay, L. D.: Fecal Retention in Children With Cystic Fibrosis: Report of Three Cases. Pediatrics 34: 72-77, July 1964.
 Jensen, K. G.: Meconium-Ileus Equivalent in a 15-Year-Old Patient With Mucoviscidosis. Acta paediat 51: 344-348, May 1962.
 Brown, P. M., Hallenbeck, G. A., Soule, E. H., and Burgert, E. O., Jr.: Cystic Fibrosis With Fecal Retention and Intussusception in Late Stages. New England J Med 263: 544-546, Sept 15, 1960.
 ReMine, W. H.: Personal communication to the authors.
- ReMine, W. H.: Personal communication to the authors.

THE USE OF POTASSIUM IN THE TREATMENT OF HEART DISEASE

Ernest W. Reynolds, Jr., MD, Ann Arbor, Mich. Reprinted from the American Heart Journal 70:1, 1965, published by The C. V. Mosby Co., St. Louis.

Potassium salts are currently used for the treatment of digitalis intoxication, and in heart failure, especially where hypokalemia has occurred after the * Associate Professor of Medicine, University of Michigan Medical Center, Ann Arbor, Mich., 48104.

aggressive use of diuretics. They are also used prophylactically to prevent losses of potassium during the long-term administration of thiazide diuretics. A few patients with myocardial infarction and coronary

artery disease have received potassium along with glucose and insulin. In order to help find the proper place for potassium in the treatment of heart disease, I have undertaken to review what is known in this field, in the hope that this might suggest where future research would be rewarding, and possibly to forestall unwarranted enthusiasm for any general application of potassium therapy.

Abnormal distribution of potassium in heart disease. Over the past three decades evidence has accumulated showing that cardiac and skeletal muscle of patients dying of congestive failure is abnormally poor in potassium, phosphorous, and magnesium, and that sodium tends to be increased.2-7 Calhoun and associates 4 further noted that potassium deficiency could be present in one ventricle but not in the other. When myocardial insufficiency resulted in pulmonary congestion, the potassium content of the left ventricle was diminished; and when myocardial insufficiency resulted in hepatic congestion and systemic edema, the potassium content of the right ventricle was decreased. They attributed the loss of potassium to overwork of the involved ventricle, noting that overworked skeletal muscle becomes deficient in potassium. Factors which would contribute to the diffusion of potassium from heart muscle in these circumstances are the associated lack of oxygen and the increased concentration of hydrogen ion.

Brown, Tanner and Hecht ⁸ have observed that patients with heart disease have a delayed excretion and a positive balance of orally administered potassium. They thought that potassium should be used with care in patients with heart disease, since these patients do not excrete potassium as rapidly as do normal patients.

Digitalis and loss of potassium. Calhoun and Harrison 9 were first to recognize that toxic doses of digitalis lowered the potassium content of ventricular muscle. This fact has now been confirmed by many investigators. Until recently, there was controversy whether therapeutic doses of digitalis caused an ingress of potassium into the heart or egress of it from the heart. Most investigators now concede that therapeutic doses of digitalis produce a small net gain in potassium by cardiac muscle, and that large and toxic doses produce a larger net loss.9-19 The amount of potassium lost from cardiac muscle increases with the dose of digitalis glycoside, and Conn 15 has suggested that one action of digitalis is inhibition of an influx mechanism of potassium. It has also been observed that the loss of potassium which occurs after the administration of large or toxic doses of

digitalis could be inhibited by the administration of excess potassium.¹³

These ideas have important therapeutic implications. It is obviously desirable to reverse by the administration of potassium the losses of cardiac potassium produced by toxic doses of digitalis. However, the hazard of producing potassium intoxication in this circumstance may be great, since less of the circulating potassium is free to enter the cellular compartment. For instance, Fisch and associates 20 have shown in experimental animals that the tolerance for intravenously administered potassium is related to the quantity of digitoxin administered prior to the injection of potassium. When potassium was administered to animals which had received an intoxicating dose of digitoxin, relatively small amounts of potassium caused a rapid rise in the plasma level of such a magnitude as to result in early cardiac standstill; whereas animals receiving only therapeutic amounts of digitoxin tolerated higher doses of potassium, with resultant lower levels of plasma potassium and fewer side effects. These data confirm the concept that large doses of digitalis block the entry of potassium into cells, but also make it evident that the threat to the organism is elevation of the level of extracellular potassium and not the total dose of potassium administered. The data also make clear the potential danger of administering potassium to fully digitalized patients with normal serum potassium; for in this instance the serum potassium may rise to high levels, producing potassium intoxication.

Potassium therapy in digitalis intoxication. Interest in the prevention and treatment of digitalis intoxication was awakened with the report by Lown and associates 21 that the amount of digitalis required to produce digitalis intoxication was related to the level of serum potassium. It was found that smaller doses of digitalis were required to produce intoxication when the serum potassium was low; and high levels of serum potassium had a protective effect in this regard. Prior studies by Loewi 22 in 1918, and Sampson and associates 23 in 1943, had reported that potassium was antagonistic to the toxic effects of digitalis, and that potassium was useful in the treatment of digitalis intoxication in man. Enselberg 24 had observed that increased A-V block was a side effect of such potassium therapy. It soon became evident from other studies that potassium was not a specific antagonist of digitalis. For instance, it was found that potassium would abolish ectopic beats equally well in patients who were receiving digitalis and in those who were not.25-26 It was also observed that, when A-V block was produced as the result of digitalis intoxication, administration of potassium did not release the block, but rather potentiated it.27-30 It was argued that potassium antagonism of digitalis was based on the rather non-specific depressing effect of potassium on ectopic rhythm. The conclusion to be reached from these studies is that the ability of potassium to suppress abnormal ectopic rhythm is nonspecific but transiently effective whether or not such abnormal rhythm is the result of digitalis intoxication. Potassium therapy is most useful when digitalis intoxication is the result of potassium depletion, for in this instance the therapeutic margin of safety of digitalis is raised by returning the serum potassium to normal. Caution is advised in the use of potassium therapy when A-V block is a manifestation of digitalis intoxication, since under these circumstances digitalis and potassium are synergistic.

Prophylactic use of potassium with thiazide diuretics. The aggressive use of diuretic agents, such as the thiazide and mercurial types, initially increases the urinary excretion of potassium, as well as sodium, and may cause hypokalemia in some patients. Weller ³¹ has presented the argument that the renal tubules of most patients and experimental animals have the ability to counteract the loss of potassium which occurs in the initial phase of thiazide administration, and can correct any resulting negative balance of potassium in spite of the continued daily use of these drugs. Prolonged thiazide treatment may result in hypokalemia without significant depletion of the cellular stores of potassium.

No evidence is available that potassium therapy is beneficial in heart failure unless there is potassium depletion. As has been pointed out, a shift of potassium from the intracellular to the extracellular compartment in heart failure is caused by the use of large doses of digitalis, and possibly is an early effect of thiazide or other diuretic therapy. The data to date do not suggest this shift is either beneficial or detrimental, unless it reaches extreme proportions, in which case it may lead to digitalis intoxication. It is common knowledge that, when severe potassium depletion occurs after excessive diuresis, supplemental potassium is beneficial. Cort and Mathews 32 observed improvement in heart failure when a severe depletion of potassium was corrected. In this circumstance the finding of a low serum potassium, a reflection of the level of extracellular potassium, is the best guide of the need for supplemental potassium. When the need for supplemental potassium arises, as indicated by an excessive diuresis, by low serum potassium, or by the electrocardiographic changes of hypokalemia, the dose of potassium chloride required will generally be higher (such as 5 to 10 Gm orally in divided doses) than the supplemental and routine dose now commonly prescribed (0.5 to 1 Gm three times a day). A normal diet generally contains 0.8 to 1.5 Gm of potassium per 1,000 33 calories and is the logical source of supply of potassium at other times.

Potassium toxicity. The toxic effects of potassium are related to the concentration of potassium at the site of action, as well as to conditions such as oxygen deficient, increased concentration of hydrogen ion, and decreased concentration of sodium, which may alter the normal potassium equilibrium across cell membranes. When potassium is administered, the rate of administration becomes important, since this will reflect the peak concentration at the site of action. A slow intravenous infusion of potassium in experimental animals induces widespread block in all parts of the heart, associated with a reduction in pacemaker automaticity until death occurs by cardiac arrest.34 Rapid infusions are attended by increased automaticity throughout the heart, leading to ventricular premature beats and ventricular fibrillation.35 Wiggers 36 has demonstrated that ventricular fibrillation of the dog's heart can be promptly stopped by large doses of potassium. This paradoxical effect of the infusion of potassium may be explained if it is assumed that the raising of the concentration of potassium to a moderately high level produces a condition of localized block throughout the heart which is favorable for the production of ventricular fibrillation. If the infusion has been rapid enough so that pacemaker automaticity is temporarily enhanced at the same time that local blocks are produced then ventricular fibrillation may be precipitated by a single ventricular beat, as suggested by Nahum and Hoff.35 If, on the other hand, the infusion is slow, the phase of increased automaticity is bypassed, and only depressed cardiac conduction and decreased pacemaker automaticity are encountered. terminal event in this case is cardiac standstill. Still larger doses may slow conduction sufficiently to arrest all cardiac activity, whether or not ventricular fibrillation is present. The end result here is profound cardiac depression.

Several reports of toxic effect in patients receiving potassium salts for digitalis intoxication are of interest in that they point out the dangers of treating digitalis intoxication with potassium when A-V block is one of the chief manifestations, and they also point out the fact that the oral use of potassium can be just as hazardous as the intravenous administration. Ac-

cording to two reports, potassium was used to treat digitalis intoxication manifest by complete heart block. In both instances, cardiac arrest resulted, leading to death in one instance and resuscitation with molar sodium lactate in the other.37 Lown 38 has commented on the dangers of treating digitalis intoxication in patients with heart failure, since hyperkalemia may result. He reports on one such patient who received 5 Gm of potassium chloride daily, and who developed atrial standstill and intraventricular block with tall T waves. Saline infusions were effective in reversing this only while the infusion was running. The patient developed pulmonary edema and died with cardiac standstill. Fisch 39 reports one case of transient cardiac arrest after the use of potassium for the treatment of paroxysmal atrial tachycardia with block caused by digitalis. Fisch 40 has also reported that the administration of potassium to a fully digitalized patient with atrial fibrillation led to complete heart block. There have also been reports of serious shock-like symptoms after the oral administration of potassium salts to patients with kidney disease, and in patients receiving only 5 Gm of potassium acetate orally who had no evidence of nitrogen retention.23

Conclusions

It is apparent from the toxicity studies available that there is a high risk involved in potassium therapy in patients with renal disease, in patients with heart failure and digitalis intoxication when the serum potassium is normal, and in patients with high-grade A-V block.

There is little evidence to suggest that potassium antagonizes any feature of digitalis intoxication, other than digitalis-induced arrhythmias. Potassium therapy is of value in the disturbances in cardiac rhythm due to digitalis intoxication in cases in which A-V block is not the chief manifestation, and in certain disturbances in rhythm which are refractory to quinidine but which are not due to digitalis. Specifically, potassium is useful in the treatment of ventricular premature beats and ventricular tachycardia, but should be withheld in cases of atrial fibrillation with highgrade A-V block and a regular ventricular rhythm. Its use in atrial tachycardia with block has proved to be of value but carries additional risks because of the presence of block. It is contraindicated in the treatment of complete heart block caused by digitalis.

The use of potassium in small daily supplementary doses to prevent the depletion of potassium in patients receiving digitalis and thiazides is unsound in most instances, and the routine use of potassium in this situation should be discontinued. Supplementary potassium may be helpful in the initial phase of diuresis in congestive heart failure and when the serum potassium is lower than normal. There should be no hesitancy about replacing potassium when there is hypokalemia, since most of the severe toxic effects associated with potassium therapy have occurred when it was used in the presence of a normal serum potassium.

- Sodi-Pallares, D., Bisteni, A., Medrano, G. A., Testelli, M. R., and DeMicheli, A.: The polarizing treatment of acute myocardial infarction, Dis Chest 43: 424, 1963. Harrison, T. R., Pilcher, C. and Ewing, G.: Studies in congestive heart failure IV. The potassium content of skeletal and cardiac muscle, J Clin Invest 8: 325, 1930. Scott, L. C.: The proportion of certain important inorganic constituents in the dying heart muscle, J. Clin Invest 9: 463, 1930.

- Calhoun, J. A., Cullen, G. E., Clarke, G., and Harrison, T. R.: Studies in congestive heart failure. VI. The effect of overwork and other factors on the potassium content of the cardiac muscle, J Clin Invest 9: 393, 1931.
- Wilkins, W. E., and Cullen, G. E.: Electrolytes in human tissues. III. A comparison of normal hearts with hearts showing congestive heart failure, J Clin Invest 12: 1063, 1933.
- tive heart failure, J Clin Invest 12: 1063, 1933.

 Iseri, L. T., Alexander, L. C., McCaughey, R. S., Boyle, A. J., and Meyers, G. B.: Water and electrolyte content of cardiac and skeletal muscle in heart failure and myocardial infarction, Am Heart J 43: 215, 1952.

 Mangum, G. H., Reichle, M. S., and Myers, V. C.: Further studies on human cardiac and voluntary muscle. Possible implication of changes in the creatine, phosphorous and potassium content, with special references to heart disease, Arch Int Med 67: 320, 1941.

- plication of changes in the creatine, phosphorous and potassium content, with special references to heart disease, Arch Int Med 67: 320, 1941.

 Brown, H., Tanner, G. L., and Hecht, H. H.: The Effects of potassium salts in subjects with heart disease, J. Lab and Clin Med 37: 506, 1951.

 Calhoun, J. A., and Harrison, T. R.: Studies in congestive heart failure. IX The effect of digitalis on the potassium content of the cardiac muscle of dogs, J Clin Invest 10: 139, 1931.

 Wedd, A. M.: Influence of digoxin on potassium content of heart muscle, J Pharmacol & Exper Therap 65: 268, 1939.

 Hagen, P. S.: The effects of digilanide C in varying dosage upon the potassium and water content of rabbit heart muscle, J Pharmacol & Exper Therap 67: 50, 1939.

 Boyer, P. K., and Poindexter, C. A.: The influence of digitalis on the electrolyte and water balance of heart muscle, Am Heart J 20: 586, 1940.

 Friedman, M., and Bine, R.: Observations concerning the influence of potassium upon the action of a digitalis glycoside (lanatoside C), Am J M Sc 214: 633, 1947.

 Wood, E. H., and Moe, G. K.: Blood electrolyte changes in the heart-lung preparation, with special reference to the effects of cardiac glycosides, Am J Physiol 137: 6, 1942.

 Conn, H. L.: The effect of digitalis and anoxia on potassium transport in the heart: Correlation with electrocardiographic changes, Clin Res 3: 111, 1955.

 Regan, T. J., Talmers, F. N., and Hellems, H. K.: Myocardial transfer of sodium and potassium: Effect of acetyl strophanthidin in normal dogs, J Clin Invest 35: 1220, 1956.

 Cairns, A. B., Jr., Love, W. D., and Burch, G. E.: The effects of acetyl-strophanthidin on the kinetics of potassium and Rb⁸⁰ in the myocardium of dogs, Am Heart J 59: 404, 1960.

 Hellems, H. K., Regan, T. J., Talmers, F. N., Christensen, R. C., and Wada, T.: The mode of action of acetyl-strophanthidin on the failing human heart, J Clin Invest 35: 710, 1956.

 Brown, T. E., Acheson, G. H., and Grupp, G.: The saturated lactone, glycoside dihydroouabain: Effects on potassium ba
- Fisch, C., Steinmetz, E. F., Fasola, A. F., and Martz, B. L.: Effect of potassium and toxic doses of digitalis on the myocardium. Circulation. Res 7: 424, 1959.

 Lown, B., Weller, J. M., Wyatt, N. Hoigne, R., and Merrill, J. P.: Effects of alterations of body potassium on digitalis toxicity, J Clin Invest 31: 648, 1952.
- Loewi, O.: Über den Zusammenhang zwischen Digitalis und Kalziumwirkung, Arch Exper Path Pharmakol 82: 131, 1918. Sampson, J. J., Alberton, E. C., and Kondo, B.: The effect on man of potassium administration in relation to digitalis glycosides,
- man of potassium administration in relation to digitalis glycosides, with special reference to blood serum potassium the electrocardiogram and ectopic beats, Am Heart J 26: 164, 1943. Enselberg, C. D., Simmons, H. G., and Mintz, A. A.: The effects of potassium upon the heart, with special reference to the possibility of treatment of toxic arrhythmias due to digitalis, Am Heart J 39: 713, 1950. Bettinger, J. C., Surawicz, B., Bryfogle, J. W., Anderson, B. N., Jr., and Bellet, S.: The effect of intravenous administration of potassium chloride on ectopic rhythms, ectopic beats and disturbances in A-V conduction, Am J Med 21: 521, 1956. Castleden, L. I. M.: Effect of potassium salts on cardiac irregularities, Brit M J 1:7, 1941. Shield, J. P., Rohrbacker, D. M., and Fisch, C.: Potassium and

- Shield, J. P., Rohrbacker, D. M., and Fisch, C.: Potassium and digitalis antagonism, (Abstract) Circulation 16: 938, 1957.

Fisch, C., Martz, B. L., and Priebe, F. H.: Enhancement of potassium-induced atrioventricular block by toxic doses of digitalis drugs, J Clin Invest 39: 1885, 1960.

Zimmerman, H. B., Gentsch, K. W., and Gale, A. H.: The action of potassium on the atrioventricular node in digitalized patients, Dis Chest 43: 377, 1963.

Fisch, C., Shields, J. P., Ridolfo, A. S., and Feigenbaum, H.: Effect of potassium on conduction and ectopic rhythms in atrial fibrillation treated with digitalis, Circulation 18: 98, 1958.

Weller, J. M.: Potassium depletion and benzothiadiazine drugs: A source of over-concern? Am Heart J 63: 842, 1962.

A source of over-concern? Am Heart J 63: 842, 1962. Cort, J. H., and Mathews, H. L.: Potassium deficiency in congestive heart failure, Lancet 1: 1202, 1954. Recommended Dietary Allowances. A Report of the Food and Nutrition Board, National Academy of Sciences. National Research Council. Publication 1146, 6th Ed Revised, 1964. Winkler, A. W., Hoff, H. E., and Smith, P. K.: Electrocardiographic changes with concentration of potassium in serum

following intravenous injection of potassium chloride, Am J Physiol 124: 478, 1938.

Nahum, L. E., and Hoff, H. E.: Observations on potassium fibrillation. J Pharmacol & Exper Therap 65: 322, 1939.

Wiggers, C. J.: Studies of ventricular fibrillation caused by electric shock. I. The revival of the heart from ventricular fibrillation by successive use of potassium and calcium salts, Am J Physiol 92: 223, 1930. Wiggers, C. J electric shock.

Somylo, A. P.: The toxicology of digitalis, Am J Cardiol 5: 523, 1960.

Lown, B., Black, H., and Moore, F. D.: Digitalis, electrolytes and the surgical patient, Am J Cardiol 6: 309, 1960.

Fisch, C., Steinmetz, E. F., and Feigenbaum, H.: Interrelationship of digitalis and potassium, J Indiana M A 56: 190, 1963.

Fisch, C., and Ridolfo, A. S.: Reverse Wenckebach block and complete atrioventricular dissociation due to potassium and digitalis, Circulation 18: 852, 1958.

ISOLATION OF THE TRACHOMA AGENT IN CELL CULTURE

F. B. Gordon and A. L. Quan, Department of Microbiology, Naval Medical Research Institute, Bethesda, Md. Proceedings of the Society for Experimental Biology and Medicine 118: 354-359, 1965.

After establishment of isolates of the trachoma agent in the yolk sac of embryonated eggs, infection of cell cultures can be readily accomplished, as indicated by appearance of inclusions.1 Growth of the agent in cell culture, however, is limited, and serial passages are regularly successful only when sonication 2 or some other method 3 is used to break up the infected cells to release infectious particles. In experiments with yolk sac established strains of agents of the trachoma. (TRIC) group, we found (unpublished observations) that the large cells produced by gamma irradiation of McCoy cell (McC)4 cultures are considerably more susceptible to TRIC strains than are unirradiated cells. The greater susceptibility is indicated by more inclusions per microscopic field, larger inclusions, detection of infectivity in higher dilutions of inoculum, and a greater infective titer of harvests from irradiated cultures.

Irradiated McC cells, in addition to embryonated eggs, were therefore used in tests for trachoma agent in a series of conjunctival specimens from suspected trachoma cases, obtained in Taiwan in collaborative investigations with personnel at Naval Medical Research Unit No. 2, Taipei. That study, concerned primarily with a comparison of cell culture and yolk sac as means of detecting trachoma infection, will be reported elsewhere. In several instances in the above study, the infective agent, demonstrated in initial McC culture by microscopic examination, was passed serially in these cells, and isolates were thus established without recourse to the embryonated egg. These results are reported herewith.

Materials and methods. The McC cell line, initiated with human synovial cells, was obtained from Morris Pollard and maintained on Eagle's medium with 10%

horse serum. When used for infected cultures, an additional 30 µM of glucose per ml was added, because of the greater susceptibility of cultures maintained in such a medium (GM) as reported previously in preliminary form.5 The culture fluid also contained 200 μg ristocetin and 100 μg streptomycin per ml. The cultures used in these studies consisted of cells that had received 5000 r of gamma radiation from cobalt-60 six to 10 days (usually 7) earlier, and had been transferred in sufficient numbers to flat bottomed tubes containing 12 mm circular coverslips to allow a complete monolayer to form. Such monolayers consist of non-multiplying cells some 2 times as large in linear dimensions as are unirradiated cells, with many possessing multiple, or multilobed nuclei. Inoculation of cultures, with 0.5 ml of specimen, was accompanied by horizontal centrafugation for 1 hour at 1600 x g, as described previously 6, to increase the degree of infection.

Four cultures were used for each specimen initially and for each passage. After 48 hours incubation at 35° C one of the coverslips was fixed in methanol, stained with a water-alcohol solution of 5% I2 and KI, and examined as a wet mount. When this culture was found positive, as determined by the presence of inclusions, the remaining tubes of the set were allowed to incubate 1-3 days. At 3, 4 or 5 days after inoculation, 0.5 ml of fresh GM was added to each tube and the cells were suspended by vigorous agitation on a Vortex Jr. Mixer. The cell suspensions were pooled and treated for 5 minutes in a sonic oscillator. After dilution, passage was made to irradiated McC cultures in the manner described above, 0.5 ml per tube, and the series was continued. The total dilution between passages was regularly 1:10. Uninfected control cultures were set up at each passage.

A 0.5 ml portion of each diluted cell culture harvest was also inoculated into the yolk sac of each of four 6-day embryonated eggs. These were observed for embryo deaths, and smears of the yolk sacs of dead embryos (or of embryos living at 14 days after inoculation) were stained by a modification of the method of Machiavello and examined. Smears were scored for prevalence of elementary bodies on a 0, 1+, 2+, 3+, or 4+ scheme, and the averaged scores were expressed numerically.

Passage from cells was usually made immediately after harvest, but when storage was necessary, equal volumes of phosphate buffer containing 0.4 M sucrose were added to the infected cell harvests and the mixture was stored at -60° C. To avoid damage to cells by 0.2 M sucrose when the stored material was passed, it was first diulted 10-fold with GM, then 2.5 ml was used as an inoculum, and after centrifugation of the inoculated tubes, the fluid was replaced with the usual 0.5 ml of GM.

Estimations were made of the number of infective particles in the inocula by counting inclusions at a magnification of 200 X. The inclusions are differentially stained with iodine by virtue of their glycogen content. When inclusions were scarce the entire converslip was scanned, but when infection was heavy a smaller portion of the monolayer was examined, usually 30 fields. The counts as given in the Tables are estimates of the numbers of inclusions in entire monolayers (12 mm diameter), many obtained by use of the appropriate factor. In previous studies (to be published) we have confirmed the validity of iodine-stained inclusion counts as a means of quantitation of infectivity, as described by Furness et al.²

Results. The cultures of 5 specimens, shown to be positive in the first passage, were used for initiating 7 series of passages, as described, which were successful in all instances.

In 5 series passage was regularly made at intervals of 3 to 4 days, often alternating. These isolates, following recommended procedures, are now designated as TRIC/TW/NMR-6/OT, /TRIC/TW/NMR-13/OT, TRIC/ /TW/NMR-15/OT, TRIC/TW/NMR-15/OT, TRIC/TW/NMR-19/OT, of which the shortened forms appear elsewhere in the text and in the Tables. In 2 instances first passage harvests were also used to initiate additional parallel series with passage at 5-day intervals. The methods for these 2 series were as described except for one added maneuver. The cells at each passage were suspended

at 72 hours, by agitation with the Vortex Mixer and immediately reset, with centrifugation, in the same tubes. This procedure (without centrifugation) has been found useful in maintaining chronically infected flash cultures.³ In these experiments it appeared to have no advantage.

Detailed data on one of the series (NMR-19, passed at 3- and 4-day intervals) are given in Table I. It may be seen that inclusion counts increased markedly as the series progressed, beginning at 41, reaching 1200 by the 6th passage, approximately 17,000 by the 9th and 10th, and nearly 50,000 at the 11th (passage 11a). A summary of inclusion counts only is given for the other series in Table II. For more accurate quantitation we use the counts of 3 or 4 coverslips; these single counts, however, with many rounded off to the nearest 10 or 100, clearly indicate the trend. In a few instances there have been marked reduction in counts between passages, the reason for which is unknown. These are seen at passage 12 in Table I, and at passage 9, for example, in the 3rd column of Table II. These can only be ascribed to some unrecognized adverse factor.

The relatively low and irregular counts seen in the two series passed at 5-day intervals (Table II) indicate that one or both of the methods used in these, different from the other series, gives relatively poor results. At some passages it was noted that the cells were in unsatisfactory condition at the 5th day.

We have observed in previous work that TRIC inclusions in very heavily infected monolayers may not take the iodine stain, and this occurred in certain passages noted in the Tables. The infection doubtless was at a high level in these passages as judged by the inclusion count of the previous passage, or by a cytopathic effect (CPE). The high incidence of inclusion was confirmed by microscopic observation. The inclusions could be recognized, when in profusion in the iodine stained monolayer, by their morphologic characteristics even though they were not differentially stained. It may be postulated that glycogen may not be formed in heavily infected cultures because of an insufficient amount of some essential ingredient.

Deterioration of cell monolayers was seen occasionally and it was obvious, from comparison with uninfected control cultures that a characteristic abnormality could be attributed to the presence of the infection. The cells tended to clump, producing drawn-out celluar processes with spaces between, giving the entire monolayer a lacy appearance. This was sometimes accompanied by release of cells from the glass surface. The degree of this cytopathic effect

did not appear to be completely correlated with numbers of inclusions, although it appeared only when the count was high, including most of those cases where the inclusions appeared not to contain gylcogen.

After these series were started we noted a report 9 from Russia that describes the isolation of an agent from trachomatous conjunctival scrapings by serial passage in chick fibroblast cells in vitro. Inclusion bodies were seen in the third passage and the series was continued through 21 passages in these cells. Seventh passage material was passed intracranially into mice and brain passages in these animals were continued. At the seventh passage mice died and elementary bodies were seen in brain smears. We made one attempt to adapt our strain NMR-19 to this host by passing a harvest of the 10th cell culture passage to mice by the intracerebral and intranasal routes. Two further (blind) passages were made with brain and lungs, with negative results.

The results of testing each cell culture harvest by yolk sac inoculation as recorded in Table I showed an irregular pattern, with little apparent correlation between the severity of infection in the embryos and the inclusion count in monolayers, produced by the same inoculum. Similar data for the other passage series took the same pattern. It is clear that adaptation to the yolk sac did not occur during the series of passages in McC cultures.

TABLE I. Data on Serial Passage of Cell Culture Isolate NMR-19 in Irradiated McCoy Cells, and Lateral Passage to Yolk Sacs.

Passage No.	Dilution	Result in cell culture (inclusion count)	Result in y. sacs D/T E.B. score	harve cell o	val to est of culture ay)
1		41	0/4	1.0	3
2	1:10	42	0/4	2.0	3
2	","	102	1/4	4.0	4
1	,,	113	0/4	1.0	3
4 5	,,	209	3/4	3.8	4
6	**	1,200	3/4	2.8	3
7	,,	1,180	2/3	2.5	4
8	**	4,900	0/4	.5	3 4 3 4 3 4 3 4 3 4 3
9	**	16,900 (CPE)	2/4	1.5	4
10	**	17,000	3/4	.75	3
11	"	I.N.	2/3	2.3	4
11a*	1:8	46,700	1/4	.5	3
12a	1:20	I.N. (CPE?)	N.D.	N.D.	_
12	"	241	1/4	1.3	3
13	"	6,300	1/2	.5	4
14	1:10	14,400 (CPE)	2/4	1.8	5
15	1:20	I.N. (CPE)	N.D.	N.D.	_

^{* =} Inoculum had been frozen and stored. Passages 11a and 12a represent a short side branch of the series, initiated with stored harvest of passage 10.

D/T = Embryo deaths/total embryos.

CPE = Evidence of cytopathic effect. See text.

N.D. = Not done.

TABLE II. Counts of Inclusions per Coverslip in Serial Passages of Trachoma Agent Isolates in Cell Cultures.

	Pas	Passed at 3 and 4 day intervals — Passed at 5 day intervals					
Passage No.	NMR-6	NMR-13	NMR-15	NMR-17	NMR-13	NMR-19	
1	77	8	680	1,100			
2	66*	68	650	247	†	697	
3	3,120	35	930	786	167	1,330	
4	12,400	120	2,550	2,690	191	133	
5	6.210	590	3,880	4,200	242	1,180	
6	3,880	480	2,300	4,640	145	763	
7	19,900	2,300	1,300	6,980	45	1,240*	
8	15,200	1,100	2,700	7,100	73	1,220*	
	16,400	130	5,800	17,000	28*	807*	
9 10	10,400	610	11,800‡	26,900	16*	I.N.*	

- * Inoculum had been frozen and stored.
- † Inclusions present, but not counted.
- ‡ Evidence of CPE.

I.N. Most inclusions were iodine negative and could not be counted satisfactorily (see text).

Comment. These results indicate that it is entirely feasible to isolate and establish TRIC agents in cell cultures only, without use of the chick embryo. A later publication will evaluate this cell culture method in comparison with inoculation of yolk sacs, for demonstration of the infection in conjunctival specimens.

Inoculation of cell culture harvests, throughout 10 or more passages, into yolk sacs gave the same sort of irregular result usually seen in the 1st or 2nd yolk sac passage from conjunctival specimens. Once an isolate has been established in yolk sacs regular deaths of embryos with 3+ or 4+ yolk sac smears is the rule. A preparation of an established yolk sac strain, with an infectivity great enough to produce 10,000 or more inclusions per coverslip, would be expected to kill embryos promptly and regularly in contrast to the results in these series. It can be assumed, therefore, that these cell culture isolates and yolk sac isolates are qualitatively different with respect to the two host systems, as a result of adaptations. Whether they differ in any other significant way, and whether the cell culture isolates possess useful characters not seen in previous isolates, is not presently known.

Summary. Five isolates of the trachoma agent have been made by culture in irradiated McCoy cells, without use of the standard method of yolk sac inoculation. These have been passed serially in cell culture at intervals of 3-4, or at 5 days, 9 to 15 times. Increase in level of infection was indicated by increasing counts of inclusions observed regularly at 48 hours after inoculation, and by cytopathic effect in some passages. Passages of cell culture harvests to yolk sacs gave irregular results throughout the series with no indication that successful passage in cell culture was accompanied by adaptation to yolk sac.

E.B. = Estimation of average relative incidence of elementary bodies in stained yolk sac smears. 4.0 maximum. See text.

I.N. = Most inclusions were iodine negative and could not be counted satisfactory (see text).

The technical assistance of C. Thomas Colonna, J. I. Thomas, and Richard Grays is gratefully acknowledged.

- 1. Gordon, F. B., Quan, A. L., Trimmer, R. W., Science, 131: 733,
- Furness, G., Graham, D. M., Reeve, P., Collier, L. H., J Gen Microbiol 23: 613, 1960.
- Mitsui, Y., Kitamuro, T., Endo, K., Matsumura, K., Science 145: 715, 1964.
- 4. Fernandez, V. M., Z. f. Zellforsch 50: 433, 1959.
- Vedros, N. A., Gordon, F. B., Bact Proc p 134, 1963.
 Weiss, E, Dressler, H. R., Proc Soc Exp Biol & Med 103: 691, 1960.
- Gear, J. H. S., Gordon, F. B., Jones, B. R., Bell, S. D., Jr., Nature 197: 26, 1963; Collier, L. H., ibid., 198: 1229, 1963.
- 8. Gordon, F. B., Dressler, H. R., Quan, A. L., Bact Proc p 132, 1963.
- Dzhumanbaeva, A. A., Bekleshova, A. Iu., Voprosy Virusologii 8: 335, 1963.

FROM THE NOTE BOOK

PARALYTIC POLIOMYELITIS—1964

During the 1964 final count of 91 paralytic poliomyelitis cases in the United States was the lowest yet recorded. This figure is less than one third of the total reported in 1963, the previous record low year. The distribution of cases was relatively uniform throughout 1964 and did not show a seasonal increased incidence in the summer and fall months as in previous years.

Geographically, the cases of paralytic poliomyelitis during 1964 were scattered. The 91 cases were reported from 83 counties; no county reported more than 2 cases during any month in the United States.

—Abstract from M&M Weekly Report 14(27): 226, July 10, 1965.

MALNUTRITION AND INFECTION

Malnutrition and infection, occurring together, are mutually aggravating and in man consistently lead to more serious disease than would be predicted from either alone. The relative importance of the various mechanisms involved is not really known. Frequently, in persons whose diets are borderline in specific nutrients, infections precipitate such deficiency diseases as kwashiorkor, avitaminosis A, scurvy, beriberi, and nutritional anemias. Most of the severe deficiencies interfere with antibody formation, phagocytic activity, tissue integrity and certain types of non-specific resistance. They may also cause changes in intestinal flora and in endocrine balance, which in turn influence resistance to an infectious agent. While it has been observed that specific deficiencies in experimental animals may have an antagonistic effect on the development of infectious agents such as viruses which are heavily dependent on metabolites of the host cell, this has not been demonstrated with the type of deficiencies occurring in man and has no apparent clinical or public health application. In man synergism is the interaction regularly observed. It is a major cause of high morbidity and mortality in underdeveloped countries where nutrition is poor

and infections common and it continues to be of importance even today for many poorly nourished individuals in industrialized countries. (Contribution number 647 from the Dept. of Nutrition and Food Science, MIT, Cambridge, Mass.)—Abstract from Borden's Review of Nutritional Research 26(2): 25–26, April–June 1965.

PREVENTIVE MEDICINE NOTES

Chapter 1, "Food-Service Principles," of the Manual of Naval Preventive Medicine, (NAVMED P-5010-1), has been revised and published under the title, "Food Sanitation." Initial distribution has been made to all ships and stations and to individuals who have maintained current mailing addresses with the Bureau of Medicine and Surgery. Individual holders of the Manual of Naval Preventive Medicine (NAVMED P-5010) who have not received the revised Chapter 1 should forward current mailing addresses to BUMED (Code 4561).

Copies of Chapter 1 are available to all who desire them. Requests should be directed to the Naval Supply Depot, Norfolk, Virginia, or Oakland, California; or to BUMED, Code 7223.—Preventive Medicine Div., BuMed.

SURGEON GENERAL'S REPRESENTATIVE VISITS FAR EAST

George H. Reifenstein MD, F.C.A.P., Director of Navy Medical Postgraduate Research and Education, visited medical facilities in the Far East area in early May of this year and represented the Surgeon General at the Fifth Far East Session of the American College of Physicians.

Enroute to Japan, Dr. Reifenstein spent several days in the U.S. Naval Hospital, Guam. Prior to the American College of Physicians meeting, he reviewed the educational training programs and examined the clinical facilities of the U.S. Naval Hospital, Yokosuka. During the College meeting, Dr. Reifenstein's warm friendliness, able grasp of a mul-

titude of medical educational problems, expert clinical judgment and outstanding pedagogical ability were demonstrated at all times.—CO, USNH, Yokosuka.

INSTITUTIONAL OUTBREAK OF PNEUMONIA

Washington, D.C. Since July 27 a total of 62 cases of acute pneumonia, 18 of them associated with the isolation of *Klebsiella pneumoniae* (Friedlander's bacillus), have occurred in a large psychiatric hospital in Washington, D.C. There have been eight deaths, most of which have occurred in cases recognized as *Klebsiella* pneumonia early in the outbreak. Postmortem examinations of six of the fatalities have shown gross pathological findings consistent with a bacterial pneumonia and *Kleibsiella pneumoniae* has been isolated from cultures of purulent material obtained from lung specimens of each of these six cases. *Klebsiella pneumoniae* has also been isolated from sputum or throat swabs of 12 other pneumonia patients.

The hospital presently accommodates nearly 6,100 patients. Those with acute pneumonia, however, have been predominantly males, many of whom are associated in a therapy group of 700 male patients. The distribution of cases according to age is consistent with the age distribution of the total population of inpatients; there have been 49 male cases and 13 female cases. No widespread minor illnesses have been reported in the hospital as a whole either prior to or during the outbreak of acute pneumonia which appeared to reach its peak in the first week of August.

Apart from the demonstration of *Klebsiella pneumoniae* in 18 cases, there has not been any other etiological agent identified up to the present time. Serological studies of acute and early convalescent serum specimens from the first 32 patients have been undertaken. So far, employing antigens for histoplasmosis, blastomycosis, psittacosis, Q fever, mycoplasma, and adenoviruses, there has been no suggestion of acute infection with any of these agents.

Epidemiological and laboratory studies are continuing. (Reported by Dale C. Cameron, Hospital Superintendent, Dr. Murray Grant, Director of Public Health, District of Columbia, and a team of CDC epidemiologists working with the staff of the Hospital and the Department of Public Health.)—M&M Weekly Report 14(31): 266, August 7, 1965.

TETRACYCLINES

Peritoneal Dialysis: It is common practice to add tetracycline to fluids used in peritoneal dialysis as a prophylactic measure against peritonitis. Studies conducted on nine severely azotemic patients undergoing dialysis with fluid containing tetracycline (25 mg/L/hr) showed that peak levels of the antibiotic were attained within 16 to 24 hours. The possibility of a systemic therapeutic or toxic effect of the tetracycline should be considered under these circumstances. The authors have discontinued the practice of adding tetracycline to dialysis fluid. They point out that most hospital-acquired infections are caused by tetracycline-resistant organisms. If peritonitis occurs during dialysis, the offending organism should be identified and a suitable antibiotic chosen. Again, consideration should be given to the possible systematic effect of the antibiotic when administered intraperitoneally.—Rose et al. (Milwaukee, Wisc), Am J Med Sci 250:66, July 1965.

Pediatric Pharmacology: The pharmacological behavior of lymecycline (a tetracycline derivative available in Europe as 'Tetralysal') is modified by age of the recipient. In newborn infants comparable doses of tetracycline resulted in relatively high blood levels, low urinary excretion, and different concentrations in various tissues. However, tetracycline has a slow diffusion rate from plasma to tissues in the very young. One exception is the brain in which comparatively high levels were observed. Other tissues known to selectively concentrate tetracycline during development are bone and deciduous teeth. It is concluded that the relative permeability to tetracycline is specific for each tissue, depending upon the age of the subject. Perhaps tetracycline dosage should be reduced for newborn infants and graded according to the tissue in which therapeutic influence of the drug is desired. - Sereni et al. (Milano, Italy), J Pediat 67:299, August 1965.—Republished from CLIN-ALERT^R, No. 219, August 17, 1965, by permission of Science Editors, Inc.

CANCER OF THE COLON AND RECTUM

Although cancer of the colon and rectum remains the second leading type of malignant disease in the United States, recent studies show that the percentage of patients living at least five years after diagnosis is rising.

This information is included in a pamphlet on "Cancer of the Colon and Rectum" issued the week of July 22 by the Public Health Service, USDHEW. It is the eighth in a series of ten pamphets on cancer

of different body sites prepared for the general public by the National Cancer Institute of the National Institutes of Health.

The improved survival rate may result partly from an increase in the percentage of patients treated by surgery, according to the pamphlet. Advances in surgical techniques and nursing care have made surgery possible for patients who formerly were considered too old, or whose disease was considered too far advanced.

The symptoms, diagnosis, and treatment of cancer of the colon and rectum are also discussed, as well as related conditions and current research. The pamphlet recommends that rectal examination with an instrument called a sigmoidoscope be included in the annual physical check-up of everyone over 40, to help detect tumors early.

Previous pamphlets in the series have dealt with cancer of the breast, uterus, skin, bone, lung, larynx, and stomach.

Single copies of "Cancer of the Colon and Rectum" (PHS Publication No. 1304) are available without charge from the Public Health Service, Washington, D. C. 20201. The pamphlet may be bought in quantity from the Superintendent of Documents, U.S. Government Printing Office, Washington, D. C. 20402, at 5 cents a copy or \$2.75 per 100 copies.

NAVAL MEDICAL RESEARCH REPORTS

U.S. Naval Medical Research Institute, NNMC, Bethesda, Md.

- Effects on Experimental Animals of Long-Term Continuous Inhalation of a Triaryl Phosphate Hydraulic Fluid: MR 005. 04–0003.1, July 1965.
- U.S. Naval Submarine Medical Center, Submarine Base, Groton, Conn.
- Time Course of Changes in Surface Tension and Morphology of Alveolar Epithelial Cells in Carbon Dioxide-Induced Hyaline Membrane Disease: MR 005. 14–3002–1. 13, January 1965.
- Dental Department Report for Deep-Freeze Four: MR 005. 12–5220–2. 15, February 1965.
- 3. Deep Freeze '61 Dental Officer's Report: MR 005. 12–5220–2. 16, February 1965.
- Bekesy Audiometry at 20 Frequencies from 2 to 6 KC Sec: MR 005. 14–1001–3. 05, February 1965.
- Selection of Men for Hazardous Duty from Indices of Individual Differences in Autonomic Nervous System Reactivity: MR 005. 14–2100–1. 13, February 1965.

- Operational Evaluation of the Various Methods of Visual Dark Adaptation Aboard FBM Submarines: MR 005. 14–2001–4. 08, February 1965.
- Visual Requirement Failure by Candidates Reporting for Basic Submarine Training During 1964: MR 005. 14–2001–3. 05, March 1965.
- 8. Carbonic Anhydrase Isozymes of Neonatal and Adult Human and Some Animal Erythrocytes: MR 005. 14–3002–10.01 Report No. 448, April 1965.
- Current Problems in Enlisted Submarine Physical Examinations: MR 005. 14–2100–1. 14, May 1965.

LABORATORY INSPECTION AND ACCREDITATION

The Commission on Laboratory Inspection and Accreditation of the College of American Pathologists has established a Laboratory Inspection and Accreditation program. Commanding Officers of Naval Hospitals are informed that this service is available on an optional basis, with fee of \$100 payable out of local funds. Interested commands should communicate with College of American Pathologists, 230 North Michigan Avenue, Chicago, Illinois 60601.
—BuMed Code 316.

MYCOPLASMA

Mycoplasma-micro-organisms appearing frequently in human and animal leukemic tissues—will be intensively studied by scientists in three institutions: University of Texas M. D. Anderson Hospital and Tumor Institute, Houston; Wistar Institute, Philadelphia; and Roswell Park Memorial Institute, Health Research Division, Buffalo. The contracts will be administered by the National Cancer Institute of the National Institutes of Health.

The studies will help determine whether mycoplasma are causally related to leukemia, whether they are contributory factors, or whether they are "passenger" agents. Studies such as these on the cause and prevention of leukemia constitute one of the four principal areas of the National Cancer Institute's special virus-leukemia program. The other areas of the program are treatment of human leukemia, the nature of animal leukemias, and the control of hazards involved in virus-cancer research.

Because mycoplasma may resemble viruses closely in size, structure, and certain chemical properties,

improved techniques must be developed to characterize and differentiate these organisms.

The studies announced will attempt to detect mycoplasma in the bone marrow and sera of leukemia patients and to correlate their presence with the course of the disease and the immunologic status of the patient. Leukemic and normal cells grown in tissue culture will be examined for the organisms, and practical methods of preventing mycoplasma contamination of cultures will be devised.

The research will also evaluate the effects of infecting mice with mycoplasma, both alone and in combination with viruses that cause leukemia in these animals. Animal cell cultures will also be infected to study the changes induced.—Abstract PHS DHEW G53, August 23, 1965.

DENTAL SECTION

NAVAL DENTAL RESEARCH REPORTS

Continuing the plan of recent issues of the U.S. Naval Medical News Letter, the third and fourth reports of the Naval Dental Corps' intramural research program, presented at the 43rd General Meeting of the International Association for Dental Research, are abstracted in this issue. CAPT F. P. Scola, DC USN, principal investigator of the SMC New London's Clinical Evaluation of Stannous Fluoride Cariostasis in Naval Personnel, is the sole clinical examiner in this study; as co-investigator, CAPT C. A. Ostrom, DC USN, conducted related laboratory studies at the Naval Medical Research Institute from 1960-1963; and currently serving as Head, Professional Branch, Dental Division, BuMed, he monitors application of this research to the Navy's Preventive Dentistry Program. Working directly in the clinical phases, CDR H. J. Keene, DC USN, has contributed effectively to several aspects of the research in caries resistant naval recruits, at the Dental Research Facility, Great Lakes. CAPT F. L. Losee, DC USN (Ret), has devoted his post-WW2 career to dental research, and is renowned for his studies on the dental influences of dietary trace elements. On 21 March 1965, he retired from active duty to join the dental research program at the Eastman Dental Dispensary and the University of Rochester. LT A. L. Coykendall, DC USN, is presently completing his Postdoctoral Fellowship at the Dental Research Facility, Great Lakes. These abstracts are reproduced with the approval of the Editor, Journal of Dental Research.

CLINICAL EVALUATION OF STANNOUS FLUORIDE IN NAVAL PERSONNEL

F. P. Scola and C. A. Ostrom, USNSMC, Groton, Conn., and BuMed, Washington D. C.

A previous report presented data on 583 naval personnel six months after one of a combination of

SnF₂ treatment methods. This report is concerned with the results from 1066 subjects after six months and from 906 after one year.

Subjects are USN enlisted men who ranged in age from 17-25 years, with clinical evidence of active caries lesions, and who were distributed randomly by age and previous caries experience into six groups at the start of the study. Annual treatment consisted of scaling, rubber cup proxphylaxis (Special pumice mixture containing 17.5% SnF₂ or NaCl), topical application (water containing 10% SnF2 or NaCl) and a dentifrice for home use (with or without 0.4% SnF2). Groups A, B, C, D and E received a topical application of SnF2 and Groups A, C, and E the SnF₂ dentifrice. Group E topical application time was 15 seconds, instead of the four-minute application time of the other groups. Group F subjects received complete placebo treatments and served as controls. The 12-month examinations revealed DMFS and DMFT increments of 3.91 and 1.04 in the control group, as compared to ranges of 1.80 to 3.45 and 0.28 to 0.91 in the five experimental groups. The combinations of SnF2 in three agents (Group A and E) were more effective than SnF2 in two or one agent (Groups B, C, D), and yielded reductions of DMFS and DMFT increments of 45 to 54 and 51 to 73 percent. Group E topical application time of 15 seconds was as effective as the four-minute application time of Group A. Reductions of similar magnitude are indicated in lesser numbers of subjects examined after 18 and 24 months.

OBSERVED AND EXPECTED GEOGRAPHIC DISTRIBUTION OF CARIES-RESISTANT NAVAL RECRUITS

H. J. Keene, F. L. Losee, and A. L. Coykendall, Dental Research Facility, Great Lakes, Illinois.

The geographic distribution of 284 white male naval recruits with negative caries histories was com-

pared with the expected distribution based on a representative sample of the recruit population at Great Lakes. Each caries-free recruit was assigned to that state in which he had primarily resided from birth to age twelve. The ratio of the number of observed to expected caries-free men was calculated for the 26 states east of the Mississippi. Florida, Indiana, Kentucky, and South Carolina all contributed 2 to 3 times the number anticipated. Maine, Massachusetts, New Jersey, and New York each presented less than one-half the expected number. The East North-Central and South-Atlantic divisions both gave observed-expected ratios greater than 1.5. In contrast, the New England and Mid-Atlantic divisions gave ratios of 0.2 and 0.4 respectively.

THE INCIPIENT CARIOUS LESION AS OBSERVED IN SHADOWED REPLICAS AND GROUND SECTIONS OF THE SAME TEETH

Mannerberg, F., Acta Odont Scand 22(3): 343-364, 1964.

This report describes the enamel changes which can be observed in the incipient caries lesion (white spots), as demonstrated by replicas of the actual enamel surface, and compared to ground sections of the original specimen. In teeth with changes in the mineralization pattern (ground section) extending up to 300 microns into the enamel, no changes from normal surface appearance were observed in replicas of the same area. In enamel with 275-500 micron deep changes in the mineralization pattern, the first changes in surface pattern were seen—the enamel prism end openings were diffuse, but the surface perikymata pattern was not altered. In two teeth with 300 and 600 micron deep mineralization changes, the surface replicas showed loss of both prism end openings and perikymata patterns. In three teeth from elderly patients, with apparently arrested incipient caries (dark stained but no clinical loss of tooth substance), the change in mineralization pattern reached a depth of 1,000 microns from the surface; and in the surface replicas, the prism end openings were absent and the perikymata alteration was only spotty.

The author classified incipient enamel caries (white spots) into five types depending on the degree of change in enamel surface and depth of subsurface mineralization changes. He discussed these changes relative to enamel surface fluoride content, presence

of the enamel cuticle, and the possibility of surface remineralization from calcium salt supersaturated saliva.

SEVERE REACTIONS TO UNINTENTIONAL INTRAVASCULAR INJECTIONS OF PENICILLIN

Popper, M., Pub Health Rep 79: 610-612, July 1964.

Accidental intravenous injections of suspensions of procaine penicillin may cause some of the severe reactions to this drug in man. The possibility of accidental entry into a blood vessel while giving an intramuscular injection can be reduced by using a technic in which the needle, detached from the syringe, is inserted into the upper outer quadrant of the patient's buttock while he is in a prone position. The needle is left in place for one minute; if no blood has appeared in the lumen of the needle, the syringe is attached and the penicillin injected.

Deliberate intravenous injection of penicillin in cats caused severe reactions and sometimes death. Some fatalities reported in the literature probably were caused by entry of some material into a vein rather than by anaphylaxis as previously believed.

The oral route is the safest method of administering penicillin. Most reactions to penicillin occur when the drug is administered intramuscularly.

A common method of giving an intramuscular injection consists of attaching a needle to the syringe, sucking up the drug to be injected, and inserting the needle on the syringe into the muscle. The plunger is next withdrawn to make sure that no blood enters the barrel of the syringe, and then the injection is made.

Suspensions of procaine penicillin, however, may block the needle in such a way that, when the plunger is withdrawn, nothing happens; when the plunger is advanced, however, the greater pressure dislodges the block, and the contents of the syringe are injected. For this reason the needle point may be in the lumen of a vein without its being detected. Obviously, this technic is not safe enough.

Many adverse reactions to penicillin result from hypersensitivity, and these reactions will occur regardless of route of administration.

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PERSONNEL AND PROFESSIONAL NOTES

Dental Officer Presentations. CAPT Gordon H. Rovelstad DC USN, U.S. Naval Dental School, National Naval Medical Center, Bethesda, Maryland, presented a Preventive Dentistry and Pedodontics seminar before the Association Odontologic Argentina 15-23 September 1965 in Buenos Aires, Argentina.

CDR Harry J. Dennis Jr. DC USN, U.S. Naval Dental School, National Naval Medical Center, Bethesda, Maryland, will present an essay entitled Preventive Concepts in Oral Surgery before the Columbus Dental Society on 27 September 1965 in Columbus, Ohio.

CAPT K. C. Hoerman DC USN, Naval Medical Research Institute, Bethesda, Maryland, visited the Zoller Memorial Clinic at the University of Chicago in June. This was a project site visit in connection with the Study Section of the National Institute of Dental Research, National Institutes of Health.

CAPT Phillip J. Boyne DC USN, U.S. Naval Medical Research Institute, Bethesda, Maryland, participated in a dual meeting of the 9th Congresso Odontologico Brasileiro and the 2nd Congresso Internacional de Odontologia held 25-31 July 1965 in Rio de Janeiro, Brazil. CAPT Boyne presented a General Course in Oral Surgery for members of the societies and participated in three symposia concerning the Use of Bone Grafts in Oral Surgery.

New Meaning Added to Active Duty for Training. The staff officers of the Naval Dental Clinic, Norfolk, Virginia, were recently privileged to hear a lecture/discussion on Oral Cytology and Diagnosis of Early Malignancies by Dr. Nelson D. Large, who was on two weeks active duty training teaching instructional methods to reserve officers at the Armed Forces Staff College.

Dr. Large comes from Rocky Point, North Carolina. He attended the University of North Carolina, graduating with an AB degree, and the Dental School at the Medical College of Virginia. For six years he held a residency in Oral Pathology at the Armed Forces Institute of Pathology where, in addition to training, he produced study sets and teaching materials. Most of the Armed Forces exhibits during that time were his productions, and there are still some of his original study sets in the registry.

At present time, Dr. Large is:

- (1) Staff Dentist at the Veterans Hospital in Richmond.
- (2) Assistant Professor of Oral Pathology at the Medical College of Virginia.
- (3) Visiting lecturer at the Dental School, University of North Carolina.
- (4) Consultant and member of the teaching team in the North Carolina State Department of Health Oral Cancer Detection Program.

Medical Department Sections of Navy Formal Schools Catalog Now Being Distributed. Navy Medical Department Formal Schools Catalog, BUMED-INST 1500.9 is now being distributed to all ships and stations having Medical/Dental Personnel. This catalog, published in accordance with OPNAVINST 1500.21, is designed to fit within the Navy Formal Schools Catalog or can be maintained separately if so desired.

Catalog of Dental Technicians Schools and Courses, NAVMED P-5029 is superseded by this publication. However, other instructions and publications pertaining to dental officer and enlisted training programs are still in effect.

PREVENTIVE MEDICINE SECTION

BUMED NOTE 6230

OCCURRENCE OF CHOLERA IN IRAN

- A. BuMedInst 6230.1D
- 1. Cholera Confirmed in Civilian Population in Iran.
- 2. Until further notice current immunization against
- cholera is required for those assigned PCS or TYD to Iran or Iraq.
- 3. Travel will be delayed only for first injection of basic series or for booster if more than six months has elapsed since completion of basic series or prior booster.
- 4. This MSG concurred with by OTSG'S, Army and Air Force.—PrevMed, BUMED.

MALARIA

USDHEW CDC Malaria Surveillance, 1964 Annual Summary, 1-2 & 17, (Received 22 July 1965).

During 1964 there was a significant increase in reported cases of malaria in the United States. A total of 171 confirmed and presumptive cases of malaria with onset of illness during 1964 were reported to the Malaria Surveillance. This represents an 80% increase over the previous 8 year average since active case investigation was established. This increase is believed to be partially due to improved methods of reporting, but probably represents a real increase in the number of cases of malaria seen in the United States.

There was an increase in the number of civilian cases of malaria in 1964, 119, and 1963, 90 cases. While in military cases were 52 in 1964 versus 58 cases in 1963. Thirty-five cases of malaria occurred in merchant seamen in 1964. Five cases occurred in Peace Corpsmen.

The majority of cases of malaria were in males in the young adult and mid-adult age range. By species, the 152 confirmed cases were: P. vivax—101 cases; P. falciparum—38; P. malariae—8; P. ovale—4; and mixed infections—1. The West African countries, Korea and South Viet Nam were the most common areas of acquisition of malaria for the cases reported in this country.

Three cases of malaria originated in the United States; two cases were classified as cryptic and 1 as induced. Though 2 of the cases were classified as cryptic, evidence in both favored introduction through an imported case as the most likely means of acquisition. If these cases truly are introduced, they represent the first autochthonous transmission of malaria in the United States in several years.

Three deaths due to malaria occurred in the United States during 1964. See chart on Page 19.

Evidence of infection by chloroquine resistant *P. falciparum* was present in 4 cases.

A review of the recommended terminology for the various modes of acquisition of malaria, and as modified to conform to recommendations of the Tenth Report of the World Health Organization Expert Committee on Malaria, is presented:

1. Autochthonous

- a. *Indigenous*—malaria acquired by mosquito transmission in an area where malaria is a regular occurrence.
- b. *Introduced*—malaria acquired by mosquito transmission contracted from an imported case in an area where malaria is not a regular occurrence.

- 2. Imported: malaria acquired outside of a specific area. (U.S.A. in this report)
- 3. *Induced:* malaria acquired through artificial means, i.e., malariotherapy, blood transfusion, common syringes.
- 4. *Relapsing:* renewal of clinical activity occurring after an interval from the primary attack greater than that due merely to periodicity.
- 5. Cryptic: an isolated case of primary malaria that is not associated with secondary cases, as determined through appropriate epidemiological investigation, including mass blood survey after the expiry of the incubation intervals.

ANEMIA SECONDARY TO PENICILLIN TREATMENT: STUDIES ON TWO PATIENTS WITH "NON-ALLERGIC" SERUM HEMAGGLUTININS

VanArsdel, Paul P., Jr. and Gilliland, Bruce C., J Lab Clin Med, St. Louis, 65: 277-285, Feb 1965. Abstracts of Current Lit on VD, USDHEW, Pub Hlth Svc., Pg. 91, No. 2 (1965).

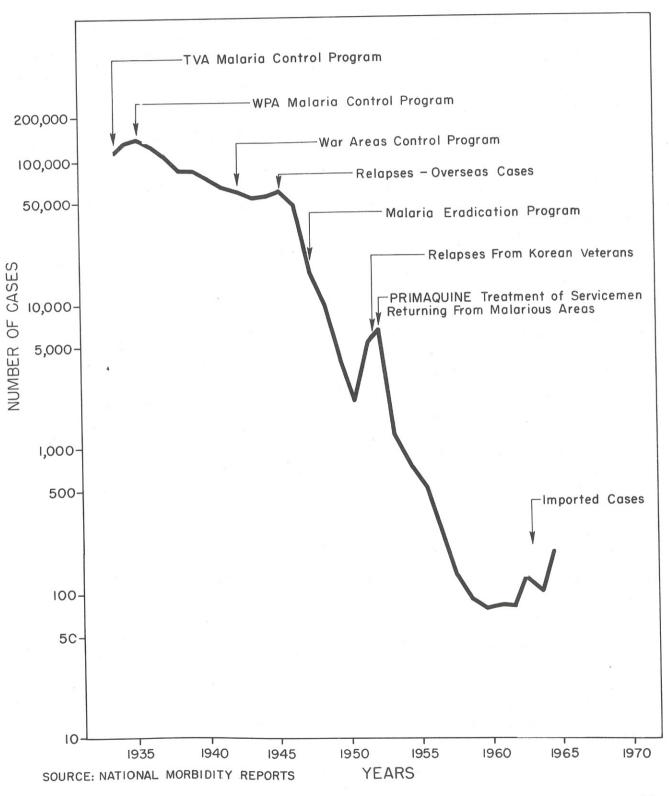
The authors discuss their study of the sera of 2 patients being treated with large doses of penicillin who developed progressive anemia, severe enough to require several transfusions. Neither patient was clinically allergic to penicillin. Antibodies which agglutinated penicillin- "sensitized" human erythrocytes in vitro were found in both cases. The hemagglutinin inhibition studies showed the sera revealed little affinity for penicillin and the more antigenic hapten, penicilloyl polylysine. Following the discussion the authors say: We are left, then, with an inadequate explanation for all the finding with these 2 sera. Their in vitro characteristics are unique, neither comparable to those of allergic sera, nor comparable to the characteristics of other hematologic drug reactions. It is hard to avoid reconsidering the possibility that the "antibody" in these patients was directed at some portion of the erythrocyte which was "uncovered" by penicillin or a metabolite.

A COCCIDIOIDOMYCOSIS OUTBREAK IN CANOGA PARK, SAN FERNANDO VALLEY

Cowper, Herbert H., MD MPH, Los Angeles County Hlth Index, 16th Report Week, ending 24 April 1965.

On Monday, 22 Feb 1965 22 boys dug a 6 foot deep hole in an empty lot near their homes. Subsequently, many of the children became ill. A variety of symptoms were present, the most characteristic

REPORTED MALARIA IN THE UNITED STATES, 1933-1964



ones being fever, cough, chest pain and rash. The illness had been shown to be coccidioidomycosis (Valley Fever).

Of the 22 children playing "war games" in the trench that was dug, 20 were clinically ill. Symptoms varied from fever and malaise alone or erythema nodosum alone to the full-blown clinical picture with fever, chest pain, rash, malaise, cough and erythema nodosum developing after the child seemed better. Two of the children playing in the trench remained asymptomatic; 1 of the boys had a positive coccidioidinskin test with a negative complement-fixation test and negative chest x-ray, the other had a negative coccidioidin skin test.

In addition, the mother of 2 of the boys subsequently became ill with fever, chest pain and rash and demonstrated skin conversion from negative to positive for coccidioidomycosis during this period of time. This woman shook out the clothing of her children when they returned from the field. The man who filled in the hole also developed typical coccidioidomycosis.

Three of the cases are interesting in that these children do not live in the area involved but were visiting on the day that the trench was being dug. One of these boys lives in Orange County and was visiting his friend in Canoga Park on 22 Feb. He was in the hole for at most 2 hours and subsequently became ill. Two other boys, who had just moved to California from Ohio on 17 Feb were visiting their cousin on 22 Feb and developed coccidioidomycosis approximately 10 days later.

Of the 24 clinically ill people, ages 6-13 years in the children and 35-40 in the adults. All of the children playing in the hole were boys. Onset of illness began from 7 to 31 days after exposure with most cases occurring from 9-13 days. The 2 cases occurring after 25 or more days from exposure had minimal exposure to the trench. Four children developed typical erythema nodosum while 13 developed an early "allergic type" rash (erythema multiforme?). Two children, who had no direct connection with the trench were also found to have coccidio-idomycosis, and they live within one block of the empty lot and may have contracted their illness through the airborne route.

Of the children and adults surveyed (26) in the area, 22 demonstrated positive coccidioidin skin tests. Among this group conversion from negative to positive occurred in 4 individuals. Complement-fixation tests were positive in 17 and chest x-rays positive in 14. The sputum from one child showed typical

spherules of *Coccidioides immitis*, approximately 6 weeks after the onset of his illness.

None of the children or adults required hospitalization. Several of the children are being watched closely because of chest infiltrations or high complement-fixation titers, but otherwise are clinically stable. Soil samples are being processed for attempted recovery of the organism. A follow-up clinic has been established at the Canoga Park Health Department to follow the progress of the children involved. Measures are being considered to eradicate the organism from the property.

Coccidioidomycosis is an endemic disease in the San Fernando Valley. An estimated 25 sporadic cases originating in this area are reported each year. Outbreaks traceable to a single exposure at one focus are unusual. More may occur than are identified.

In this outbreak, symptoms were originally ascribed to respiratory viruses. The skin rashes which occurred later and which physicians could not satisfactorily explain compelled the investigation.

This disease has occurred in outbreaks in several other areas of this County, e.g., rural areas around Saugus and Newhall in the Susana Mountains. There have been no recorded outbreaks in the Antelope Valley.

BOTULISM ON QUEEN CHARLOTTE ISLANDS, BRITISH COLUMBIA

Director, Epid Dept of Hlth Serv and Hosp Ins, Victoria Brit Columbia, 20 Oct 1964. Ottawa, Canada, Epidemiological Bull., 8(10): 78, 1964.

A case of botulism has been reported from Bella Bella in the Queen Charlotte Islands, British Columbia. A native Indian woman, age 37, was admitted to the hospital at Bella Bella on 3 Sept 1964, with a history of having eaten between 100 and 200 ccs of putrified salmon eggs 24 hours previously.

She complained of diplopia, dysphagia, weakness, fatigue and faintness. She had vomited once about 8 hours prior to admission. There was very little objective evidence of any neurological disturbance, but she did vomit again during the first 24 hours in the hospital. As she remained very lethargic and continued to complain of diplopia and dysphagia, 40 ccs of tetravalent botulinum antitoxin were administered the day after admission. In a day of receiving the antitoxin she showed considerable improvement, and her neurologic complaints gradually disappeared. Her appetite improved over the next week.

A toxigenic strain of type E Clostridium botulinum was isolated from the vomitus as well as demonstra-

tion of botulinum toxin in the vomitus samples and blood of the individual. The woman was the only person who sampled this particular batch of salmon eggs. The relatives were instructed to destroy the remainder.

Some interesting information about the preparation of "stink eggs" has been obtained from one of the older native women in Bella Bella: The salmon roe is collected in August and placed in containers, sometimes as large as 5 gallons. The eggs are washed repeatedly in fresh water until completely free of blood and the red jelly-like matrix in which they are embedded. They are then salted with about 2 table-spoons of salt to a quart of eggs and left to stand, covered or uncovered, about 5 days. Then the eggs are sampled, and if they leave a "dirty" taste in the mouth they are left for another day or 2 at which time they are "really good" The eggs may be kept for up to 5 months.

The Indians have their own ideas as to what renders the "stink eggs" occasionally harmful. The roe next to the liver, which has a yellowish tinge, they say, must be removed and it should not be stored in metal containers.

The eating of putrified salmon eggs at one time was forbidden, but now "stink eggs" are once again a delicacy widely enjoyed by young and old alike at this time of the year. There is hope that the practice may die out in another generation or so as the younger women do not seem to have mastered the art of preparing the dish.

AIR POLLUTION IS A COSTLY LUXURY

The Health Bulletin, Official Pub of the North Carolina State Bd of Hlth, Nov 1964, pp 13-14.

In the early days of our industrial development, the belching smokestack was a symbol of progress and prosperity, a symbol of a young nation on the way to greatness. Today, we are learning that it is possible to have both prosperity and clean air. Indeed, we know that in many ways air pollution is the enemy of prosperity. We know that with our burgeoning technology it has come to mean many different kinds of contaminants, drifting and sifting across state and local boundaries, hastening the deterioration of buildings, damaging crops, injuring health.

Air pollutants come not only from the exhaust pipes, the carburetors, the crankcases, and the gas tanks of automobiles, trucks, and buses; they also come from home heating plants and backyard burning

of leaves and trash; and from hotel and apartment incinerators.

They come from burning municipal dumps, burning auto bodies, and burning waste from building demolition; from commerical enterprises such as drycleaning and restaurant kitchens, from cement-mixing and asphalt-paving operations.

They come, in large volume, from oil refineries, power plants, steel mills, pulp and paper factories, and almost every other kind of factory.

Of immediate concern to us are the effects already being produced on man and property by local and regional changes in the air due to our loading it with harmful pollutants.

Agricultural losses alone in this country are estimated at approximately \$500 million a year. Current estimates of total economic damage caused by air pollution run as high as \$65 per person per year, or some \$11 billion annually.

Costliest of all the penalties we pay for dirty air, of course, is the toll it exacts in human health. Contaminated air can actually shorten our lifespan.

The evidence is coming in slowly, as our research continues, but there is already enough to establish a definite link between air pollution and the frequency and severity of many diseases, mostly respiratory and mostly chronic. These include not only the common cold, chronic bronchitis, and bronchial asthma—but also two of our most dreaded and most rapidly increasing diseases: Emphysema and lung cancer.

Here, then, are three admonitions which experts in this field give:

- 1. We should not postpone action until emergency makes it compulsory.
 - 2. We cannot purify the air after it is polluted.
- 3. We cannot clear the air without close cooperation—among all levels of government, industry, and the public.

The State Board of Health has recognized the expanding problem of Air Pollution and the potential harmful effects on human health. To secure more information as to the extent of the problem and to determine to some degree the quality of the air we breathe, a study was made in August 1958-March 1959 with the assistance of the Public Health Service.

Thus in 1963, a request was presented to the General Assembly for legislation which would authorize the State Board of Health to engage in an Air Hygiene Program.

The General Assembly favored this request, and the State Air Hygiene Program Act was passed. Because of the late passage of the act, no appropriation was made to carry out the provisions of the act. A request has been submitted to the Advisory Budget Commission for funds to implement this law.

With no special funds and by using limited engineering service, some work has been started. Six short-term sampling programs were conducted. A number of sampling stations were established. Assistance has been given local health departments in investigating complaints and helping to solve local problems.

With financial support from our 1965 General Assembly, we will be able to assign the personnel needed for this program and really begin to do something about protecting our air resources.

Air Hygiene was given statewide and nation-wide emphasis by the observance of "Cleaner Air Week" the last week in October.—Sanitation Section, PrevMed Div, BUMED.

MILKER'S NODULES

DNHW EPID DIV ALBERTA, Ottawa, Canada, Epid Bull 9(2): 17, Feb 1965.

Six persons contracted lesions on the hands after milking cows that had suffered from lesions on the teats, were reported to the Grande Prairie Health Unit, Alberta, Canada, in October and November 1964.

A female, 23 years old, had been vaccinated 15 years previously, and had several white blister-like lesions containing a small amount of fluid on the back of both hands. Swabs from the lesions were bacteriologically and virologically negative. A second case, also previously vaccinated, but seen in a later stage of the infection, showed round, yellowish, hard, elevated lesion about 2 centimeters in diameter on the thenar eminence of the right hand. The other cases had raised, nodular lesions, bluish in color, with a papular surface. It seems likely that these cases were varied manifestations of milker's nodules which is caused by a virus of the pox group. Although similar in some respects to the classical cowpox and vaccinia virus, they do not confer reciprocal immunity. No cases of generalized infections of this type were reported.

NEW TYPE OF ACCIDENT

Byron, Alan J., The Royal Hospital, Sheffield, England. Brit Med Jour 1(5428), 192, 16 Jan 1965.

In the last few months a new type of industrial accident is becoming manifest. This is no less than avulsion of a wide area of hair and sometimes scalp.

The phenomenon is exclusive to young men obsessed with the present day "Samson complex" of allowing their hair to grow to extraordinary lengths. The result is that it becomes inextricably entangled in moving machinery with, for them, disastrous consequences.

The patient was a boy of 17 with hair of average length 9 in. (23 cm). He is employed as a machinist at a cutlery firm and the accident occurred while working at the machine, when his hair became entangled with a rapidly revolving turret lathe. As his head was pulled towards the machine he violently jerked his head away. A substantial wedge of hair was avulsed measuring some 5 in. by 2 in. (13 by 5 cm.) but no scalp was removed with it. There was some serous oozing from the denuded area. The scalp was cleaned well with Cetavlon solution followed by eusol. The damaged area healed uneventfully and fresh hair is slowly growing. He has not as yet, alas, had a haircut.

It is felt the legislation compelling women to wear hair nets be extended to men of hair length beyond a reasonable figure.

Editor's comments. Article 1161.1.b, U. S. Navy Uniform Regulations, states "Hair shall be worn neatly and closely trimmed. The hair may be clipped at the edges of the sides and back, but must be so trimmed as to present an evenly graduated appearance, and shall not exceed 3 inches in length." Safety first!

AIR POLLUTION LINKED TO EXCESS DEATHS IN NEW YORK

Environmental Hlth Ltr, 4(18), July 1,1965.

A team of researchers from Albert Einstein College of Medicine has reported that heavy air pollution was a major factor in causing 647 more deaths than usual in New York City between Jan 29 and Feb 12, 1963. The study implicated, more precisely, the combination of air pollution with an epidemic of Asian influenza and extreme cold.

But the study found that air pollution, when added to other causes, is responsible for more deaths than the other causes acting alone. When pollutant levels were tolerable, deaths exceeded the average by 242; thus the combination of pollutants and clinical causes could be said to account for an additional 400 excess deaths, according to the survey.

The report was presented to the Air Pollution Control Association meeting in Toronto by Dr. Leonard Greenburg, chairman of the Department of Environmental Medicine.

Meanwhile, a special committee of the New York City Council which has been studying air pollution for several months reported that pollution was a contributing factor in the increased death rate from respiratory diseases and lung cancer.

Merely breathing the city's air causes as much inhalation of benzpyrene as smoking two packs of cigarettes a day, and more sulfur dioxide is present in New York than in any other major city, according to the report of the committee headed by Robert A. Low.

ACID STREAM POLLUTION FOUND HEAVY IN APPALACHIA

Environmental Hlth Lt, 4(18), July 1, 1965

Some streams in the 10-state Appalachian area contain very large amounts of acid and waste originating in coal mines, the Interior Department's Geological Survey reports.

The wastes and acids have deleterious effects on plant and marine life and limit the usefulness of these streams for future industrial use, the Survey reported after its hydrologists traveled 17,000 miles of highways from Pennsylvania to Alabama in studying more than 300 streams. Nearly all major streams affected by acid-mine drainage are located in Pennsylvania, West Virginia and Ohio.

"Of 72 streams sampled in Pennsylvania, 22 were acid," said S. K. Love, Chief of the Survey's Quality of Water Branch. The acid load discharge ranged from two tons per day at McGees Mill on the West Fork of the Susquehanna River to 240 tons per day at Vandergrift on the Kiskimenetas River.

In West Virginia 14 of 56 streams sampled were acid, with a range of .3 to 41 tons per day; Ohio had seven of the 37 streams sampled acid with a range of 1.5 to 41 tons. Despite the high acidity, the study showed that a majority of streams sampled in Pennsylvania, West Virginia and Ohio have water of good quality.

HYMENOLEPIS DIMINUTA (RAT TAPEWORM) INFECTION IN MAN

Edelman, Morton, H., MD, Spingarn, Clifford L., MD, Nauenberg, Walter G., MD, and Gregory, Charles, Am Jour of Med 38(6): 951–953, June 1965.

The occurrence of the rat tapeworm, *Hymenolepis diminuta*, as a parasite of man is infrequent and its incidence in the United States is only 0.03 to 0.07%.

Cases in man have been encountered most frequently in Georgia, Tennessee and Texas. Its distribution is worldwide and cases have been reported from South America, Australia, Europe, the Far East, India, Mexico, Canada and South Africa.

In routine examinations of stool specimens for intestinal parasites in patients attending the Parasitology Clinic of The Mount Sinai Hospital, a case of rat tapeworm infection was discovered in a young boy. Because of the role of rodents and insects in the transmission of this infection and the possibility that other cases of this type may be observed, the epidemiology, clinical features, treatment and prevention of this disease were reviewed.

Case Report

A 6-year old Puerto Rican boy, who has lived in the United States since the age of 1, was examined in the Pediatric Clinic of The Mount Sinai Hospital in April 1962 because of complaints of fever and cough. He had been having frequent upper respiratory tract infections, and for several months anorexia, abdominal pain, listlessness and failure to gain weight had been noted. Physical examination revealed a small boy, not acutely ill. The oral temperature was 100.4° F., weight 42 lbs., height 45". Examination of his lungs revealed occasional rhonchi at both bases. The remainder of the examination, including that of the abdomen, did not reveal any abnormalities. Laboratory studies showed 12.9 gm. % of hemoglobin, and a white blood cell count of 7,300 per cu. mm. with 40% polymorphonuclear cells, 39% lymphocytes, 2% atypical lymphocytes, 7% monocytes and 4% eosinophils. The urine contained a trace of albumin, the test for sugar was negative, and there was a normal microscopic sediment. A chest roentgenogram revealed slight distortion of the markings in both lower lung fields, more on the right than on the left, with associated basilar emphysema. He was treated for bronchitis. When he returned to the clinic shortly thereafter, his respiratory symptoms had subsided. In the interval, he had submitted 3 stool specimens for routine parasitologic examination, and all 3 specimens showed ova of Hymenolepis diminuta. On questioning, it was learned that his home was heavily infested with rodents and cockroaches.

He was transferred to the Parasitology Clinic and treatment for the rat tapeworm infection was given. The drugs used were administered at intervals of 2 to 4 weeks in the usual doses for his weight and age. The infection was found to be resistant to the following agents: piperazine citrate 500 mg. twice daily

for 7 days, quinacrine hydrochloride 100 mg. daily for 5 days, dithiazinine iodide 50 mg. 3 times a day for 7 days and chloroquine phosphate 250 mg. daily for 5 days. The infection was subsequently treated successfully with oleoresin of aspidium, 4 ml. Five stool specimens examined at weekly intervals were negative following completion of this treatment.

Comments

The rat tapeworm is a small cestode, measuring 20 to 60 cm. in length with 800 to 1,000 proglottids. The scolex is club-shaped, and has a rudimentary unarmed rostellum, and 4 small suckers. The ovum is subspherical, yellow brown in color, and measures 60 by 80μ . It has transparent outer membrane and an inner membrane around the oncosphere which contains 6 lanceolate hooklets arranged in a fan-shaped pattern. It is twice the size of the ovum of *Hymenolepis nana*, the dwarf tapeworm, which has 4 to 8 thread-like filaments arising from each of the 2 polar thickenings of the inner membrane. Gravid proglottids become detached from the strobila, disintegrate and discharge their eggs which are passed in the feces.

The rat tapeworm is a common parasite of rats and mice in the United States. Various species of larval and adult insects (rat fleas, myriapods, beetles, lepidopterans, millipedes and cockroaches), which are scavengers in their habits, serve as obligatory intermediate hosts. The cysticeroid larva develop in the intestines of these arthropods of the worm into a cercocystis. The ingestion of the parasitized intermediate host causes infection of the definitive murine host. Man is infected accidentally by ingesting food (dried fruits, cereals) contaminated by a parasitized insect, or by swallowing ectoparasites of the murine host. In the definitive host (rodent or man), the cercocystis is liberated and the scolex becomes evaginated and attaches itself to the duodenal or jejunal mucosa and grows to an adult stage in 18 to 20 days. Several adult worms may be present in a host.

A review of the literature revealed that cases of this infection have been reported from all parts of the world. Riley and Shannon in 1921 were able to collect 61 cases. Keller reported 8 cases from Tennessee. It is of some interest that few reports have appeared in recent years, and no record could be found of a report of an authenticated case from New York State. Chandler, in a survey of 10,000 examinations in India, found 23 cases of *Hymenolepis diminuta*. In a series of 10,000 specimens examined in our laboratory since 1961, only this one instance of this infection was encountered.

The rat tapeworm, an inhabitant of the upper small intestine, is said to produce a catarrhal enteritis. As a rule, there are mild digestive symptoms but with heavier infections, epigastric pain, anorexia, diarrhea and nervous symptoms are said to occur. In some instances, there are a mild anemia and an eosinophilia of 4 to 16%. Occasionally an enterocolitis is present, causing 4 to 6 loose movements daily, often containing blood.

The diagnosis is made by finding the characteristic ova of *Hymenolepis diminuta* in the stool. Detection is facilitated by the use of sedimentation technics. Occasionally proglottids, or the entire adult worm, may be passed spontaneously or after the administration of a cathartic.

The therapy of rat tapeworm infection is generally successful with drugs effective against other cestodes. Oleoresin of aspidium is the drug of choice and was given in this case after failure to respond to the other drugs used, namely, piperazine, quinacrine, dithiazanine and chloroquine.

Prevention of this infection may be accomplished by anti-rodent campaigns. The spraying of homes with appropriate insecticides will destroy infected rodent fleas, meal worms and beetles around human habitations. Eradication of cockroaches in homes eliminates another possible source of infection. Protected storage of foods such as precooked cereals and dried fruits is essential to reduce the incidence of contamination with the parasite.

Summary

A case of *Hymenolepis diminuta* (rat tapeworm) infection is described in a young boy residing in New York City.

A brief resume of the epidemiology clinical features, treatment and prevention of this disease and bibliography is presented.

KNOW YOUR WORLD

Did You Know:

That the first large-scale study ever made to determine possible relations between long-term health effects in the use of pesticides was begun in March 1965 by the Public Health Service?

The study, begun in 9 States, is expected to be extended next year to at least 3 other areas. Initial cost will be \$1.2 million and will rise to \$2.3 million in 1966. The research will continue for 5 years in all areas.¹

That WHO and UNICEF have undertaken to help the Government of El Salvador with a 4 year tuberculosis control project in the Province of Usultuan?

It is planned to apply the experience gained in the project—which will cover about 182,000 persons throughout the country until the disease ceases to be a public health problem in El Salvador.

WHO will provide a tuberculosis consultant and award fellowships for the training of Salvadorean doctors in control techniques. UNICEF will provide supplies and equipment; local costs will be met by the Government.2

That wild animals with rabies have been crossing the East German frontier to West Germany? In the province of Schleswig-Holstein the migration has already given rise to anxiety among public health authorities. At present, however, the most serious situation in Germany is that in the Bavarian Forest. It is not clear whether the rabies wave is really coming from Thuringia, East Germany, or whether it is the result of the movement of wild animals into Germany from Czechoslovakia, where the incidence of the disease is relatively high.3

That in the first 9 weeks of this year, 22 cases of acute poliomyelitis were reported in Hong Kong? Three of these proved to be fatal. The incidence of poliomyelitis this year is higher than would be expected since in 1963 an extensive vaccination program was begun which is still in progress.4

That a measles epidemic of unknown proportions has been reported among Eskimos in the settlements of Port Harrison, Povungnituk and Sugluk, East Coast of Hudson Bay, Canada?

The epidemic began 19 May 1965; an infant has died up to 2 June 1965. Since the beginning of the epidemic followed very closely with crash measles vaccination programs, it was thought that the illnesses came as the result of the vaccination itself. As the East Coast of Hudson Bay at that time was in the throes of a spring breakup, it was impossible to influence the epidemic from the outside. The community of Fort Chimo was vaccinated in 1963, and Baffin Island will be vaccinated in the summer of 1965. A full scale vaccination program will be undertaken.5

References

- 1. DHEW PUB Hlth Rpt, 80(5): 388, May 1965.
- WHO Chronicle, 19(4): 161, Apr 1965.
- JAMA, 193(2): 179, 12 July 1965 (Med News, London, 30 April 1965).
- 4 JAMA, 193(2): 179, 12 July 1965 (Med News, London, 2 April 1965).
- 5. Dept Nt'l Hlth & Welfare Epid Bull, Ottawa, Canada, 9(6): 53, June 1965.

EDITORIAL DESK

OPERATIONAL MEDICINE REFRESHER SERIES

INTRODUCTION

With global deployment of Navy and Marine Corps personnel, the Navy physician is finding that a knowledge of the principles of preventive medicine and public health is necessary if he is to do a good job. The knowledge of these principles and the techniques of their application constitute a medical specialty with which many medical officers, particularly those newly commissioned, are unfamiliar. This is easily understood. The United States possesses a highly organized public health system which has helped to develop standards of sanitation and hygiene and communicable disease control unequalled by any nation in the world; but leave the United States for some of the underdeveloped countries and, from the public health standpoint, go back a few centuries in time. The practicing physician in Sipsey, Alabama, need not concern himself with malaria-yet this disease is still the world's leading cause of death. The physician practicing in a suburb of New York City is concerned with water because there is a shortage and he cannot water his lawn-he does not have to worry about its containing amebic cysts of Schistosoma cerariae, or live vibrio comma organisms; but the military physician in Da Nang, Viet Nam, is vitally concerned with malaria-he sees cases every day. He must assure procurement of safe water-amebiasis is no stranger to his practice.

Recognizing the need for a better preventive medicine and operational medicine orientation among Navy Medical Officers, the Surgeon General of the Navy has requested that the Preventive Medicine Division of the Bureau of Medicine and Surgery prepare a series of short articles for publication in the U.S. Navy Medical News Letter. These articles will deal with communicable disease control, tropical medicine, water, food, and general sanitation, control of insect and animal pests and disease vectors, and general health practices. An attempt will be made to present specific useful information and the reader will be referred to applicable BUMED Instructions, technical publications and other appropriate sources where indicated. While primarily directed to those physicians going into Southeast Asia and other underdeveloped areas, most of the information presented should be of value to the shipboard medical officer and to others at stateside Navy facilities. Always keep in mind that the U.S. Navy Preventive Medicine Units, including one in Viet Nam, are available to you for consultation and assistance.

The first article is on malaria.

MALARIA

Malaria is an acute and chronic infectious disease characterized by intermittent chills and fever, splenomegaly, debility and anemia. There are four species of the genus Plasmodium which produce this disease: P. vivax, P. malariae, P. ovale, and P. falciparum. The disease produced by the latter species is not infrequently fatal. The often mortal complication of falciparum malaria, termed "black water fever," results in a massive hemolysis leading to shock, collapse, and "lower nephron nephrosis" (see "Hemodialysis in the Management of Acute Renal Failure," U.S. Navy Medical News Letter, 44:(11), 11 Dec 1964). For a comprehensive coverage of malaria, the interested reader is referred to a text on tropical medicine. (One that is highly recommended is the Manual of Tropical Medicine by Hunter, Frye, and Swartzwelder). Another excellent publication is NAVMED P-5052-10, "Malaria, Clinical Features, Treatment, Control, and Prevention."

With a disease such as this, it is always better to prevent it; and actually malaria prophylaxis programs are generally very effective when the schedules are faithfully adhered to. The combined Chloroquine-Primaquine phosphates tablet (FSN 6505-854-2239, and FSN 6505-753-5043, chloroquine 300 mg base and primaquine 45 mg base) administered one tablet weekly while in a malaria endemic area, and for 6 weeks at one-weekly intervals after leaving an endemic area is an effective preventive measure. One should keep in mind that primaquine can produce a hemolytic reaction in sensitive individuals and this is rarely caused by the levels of primaquine contained in the current prophylactic dose.

BUMED Instruction 6230.11 D, Subject: Malaria; control and prevention, gives the complete recom-

mended prophylactic regimen and should be referred to by all medical officers operationally concerned with malaria prevention.

The matter of drug-resistant falciparum malaria is a very complex one. In 1961, chloroquine-resistant strains were first demonstrated to be present in Southeast Asia. Now, the existence of quinine-resistant strains has also been documented from Viet Nam. This creates a real challenge to the clinician who handles these cases.

The course of chloroquine-resistant malaria has the potential of differing from patient to patient because of the normal biological variation which may be seen in the host-parasite relationship. Generally though, the pattern has been that the individual patient when first attacked experiences a good clinical response to the usual therapeutic levels of chloroquine. There is reduction of fever and reduction of parasites in the peripheral blood, and ostensibly, the patient is cured. Then anywhere from 4 to 10 days later, there is a relapse. Again, upon treatment with the usual doses of chloroquine, the clinical symptoms may disappear. Usually on the first relapse the total parasite count is high, but with clinical doses of chloroquine the count goes down. Still, one may be able to find a few parasites even though there are no clinical symptoms (the patient may become asymptomatic for a period until a second relapse occurs and it is usually during this time when therapeutic levels of chloroquine are ineffective against the parasites). This is probably what happens—by the time the individual reaches the hospital-he has already had 2 or 3 attacks. If a patient with severe symptoms of falciparum malaria is given 11/2 grams of chloroquine and within 3 hours there is no reduction in the blood parasite count, one should not wait for the other studies, but should immediately institute quinine therapy.

Experience with the Thailand strain of chloroquine-resistant *P. falciparum* malaria indicates that 540 milligrams of quinine base in a single dose, although not curative, exerts a pronounced schizonticidal effect. A curative regimen should consist of no less than a total of 8 grams of quinine given at the rate of 2 grams daily.

While the existence of quinine-resistant strains has been documented, the incidence or frequency of these strains in Viet Nam are not known. One strain of quinine-resistant *P. falciparum* from Viet Nam that was studied was also found to be chloroquine-resistant. However, it was sensitive to pyrimethamine (Daraprim). To further compound the problem though, the Army has reported strains from southwest of Saigon that are resistant to all synthetic

antimalarials and quinine. With these strains, it has been found that combinations of sulfadiazine plus a sulfone (diaminodiphenylsulfone or DDS, the antileprosy drug) produce a cure. Dose schedules:

- a. 4 grams sulfadiazine daily for 6 days together with 100 milligrams of DDS daily for 6 days; or
- b. 50 milligrams of pyrimethamine (Daraprim) daily for 3 days plus 100 milligrams of DDS daily for 6 days.

To summarize, there are 4 types of *P. falciparum* malaria:

- 1. Chloroquine sensitive strain.
- 2. Chloroquine-synthetic antimalarial resistant *P. falciparum* malaria but responding to quinine.
- 3. Chloroquine resistant-quinine resistant strains but sensitive to pyrimethamine (Daraprim).
- 4. Resistant to all synthetics and quinine but responding to combinations of sulfadiazine and diaminodiphenylsulfone (DDS).

It is strongly felt that when a case of *P. falciparum* is diagnosed, the patient should not be sent back to full duty until he has had a parasitemia-free period of at least 2 weeks. Medically, this is good practice.

P. falciparum malaria is a very serious disease when untreated and one with a high mortality rate. The differential diagnosis may be very confusing because P. falciparum malaria can stimulate enteritis, upper respiratory disease, dengue and many other diseases. One has to have a very high level of suspicion to permit early diagnosis and treatment. If there is any question as to chloroquine response, adequate amounts of quinine must be administered immediately.—Head, Tropical Diseases Branch, PrevMedDiv, BUMED.

A CAREER DEVELOPMENT PROGRAM FOR HOSPITAL CORPSMEN AND DENTAL TECHNICIANS

By LCDR C. "B" Longest, MSC USN, Head, Procurement and Training Branch, Medical Service Corps Division, BUMED.

This article describes a career development program for hospital corpsmen and dental technicians who desire a naval career in a commissioned status in the Navy Medical Service Corps.

A commission in the Supply and Administration Section of the Navy's Medical Service Corps awaits the energetic and competent hospital corpsmen and dental technicians planning to pursue a military career.

As the need for administrative and managerial skills continue to increase within our society, it necessarily follows that the requirement for such abilities are increasing within the military setting. Officers of the Supply and Administration Section are trained and experienced in the many facets of medical and institutional supply, personnel management and patient affairs, food service, maintenance, all fiscal matters, and public relations, and are assuming an even greater responsibility in the administration of the Navy Medical Department. Therefore, officers selected to perform such important duties must possess the abilities to discharge their responsibilities effectively and efficiently. To accomplish this objective, the concept of "promotion from within" is readily apparent as reflected by the procurement policies governing the replacement of more than 95% of the annual officer vacancies in the Supply and Administration Section of this Corps. Each year selection for these appointments are made from senior enlisted hospital corpsmen and dental technicians serving on active duty in pay grades E-6 through E-9. This article, therefore, is addressed to those hospital corpsmen and dental technicians who are desirous of achieving commissioned status in this section of the Medical Service Corps.

How does one apply for such an appointment? By meeting the criteria outlined in BuPers Instruction 1120.15 series. No instruction, however, can outline in specific detail the combination of all factors that ultimately lead to such an appointment. The most significant factors are controlled by the individual concerned, and without proper preparation for such an important step in career planning, you will be at a disadvantage in competing with the many outstanding personnel aspiring to appointment in the MSC. You, as a junior hospital corpsman or dental technician whose ultimate goal is to obtain commissioned status, should develop and pursue a well-planned, self-improvement program early in your career. This may be done in various ways, such as, actively participating in Navy or USAFI correspondence course programs or, the enrollment in part-time, offduty courses of instruction at civilian institutions when the opportunity to do so is present.

In applying for a commission under this program the first, and generally considered the most difficult hurdle you must overcome is the Officer Selection Battery Test (OSB). Unless you score a relatively high mark on this examination, you cannot hope to progress further in your quest for a commission. Therefore, it is necessary that you begin preparation early in your career for this examination which is

designed to measure your educational background and ability. For the past three years approximately 600 candidates applied each year for an average of 50 vacancies in the Supply and Administration Section of the Medical Service Corps. About 50% failed to achieve a high enough score on the OSB to continue in the program.

One aspect of the OSB which seems to prove the biggest stumbling block for many applicants is the mathematics section. This portion of the exam includes a wide variety of mathematics, progressing from simple arithmetic through algebra, geometry, and trigonometry. A complete, basic knowledge of mathematics is a prerequisite to the successful completion of this portion of the exam. You can prepare yourself through a program of self-study, utilizing USAFI courses or other available means mentioned earlier. One particularly useful tool of study, and an enjoyable one, is doing mathematics for fun. The quiz in Navy Times, for example, provides an excellent means of gaining proficiency in this area.

Another area in which some candidates have encountered difficulty is the English section wherein reading comprehension and word study are emphasized. Reading can be the key to this problem, for it is through reading that man gains knowledge. As you read, make an effort to learn and if you encounter a word you do not recognize, look it up. Do word problems, crossword puzzles, or avail yourself to special self-study texts on this subject.

In addition to the areas described above, the Officer Selection Battery Test covers subjects such as naval knowledge, history, social sciences, and physics. In short, as described earlier, it is a comprehensive evaluation of the candidate's general knowledge. By thorough preparation you can fortify your knowledge and participate in the OSB test series with more self-confidence in continuing your application processing for a commission. The BuPers Instruction previously mentioned also lists a recommended course of study in preparation for the OSB.

In any adventure we might say that "proper preliminary planning prevents poor performance." This philosophy can well apply to the development of a naval career.

Although successful completion of the OSB is an important factor in the MSC in-service procurement program for Supply and Administration officers, you will also be required to take a written professional examination designed to determine your knowledge in all fields related to Medical Department administra-

tion. This examination will include general Navy organization and administration, customs and usages of the services, and Medical Department administration, including, but not restricted to the areas of: personnel administration, patient affairs, fiscal and supply, food service, military justice, and general Navy orientation.

Applicants should be prepared to write an essaytype examination where, given a set of facts, they must display the ability to recognize the problem, think of the concepts involved, and write a logical solution. It is in this examination that preliminary planning and experience is of vital importance. As you prepare for the OSB by studying particular subjects, so must you also ready yourself for the professional examination. However, this examination is specifically related to your duties within the Medical Department. You may study the Manual of the Medical Department, the Bureau of Naval Personnel Manual, Navy Regulations, the UCMJ, and numerous other manuals and publications. The most important single factor in successful completion of this examination, however, is in long-term planning. Study should begin at an early point in your career through such efforts as correspondence courses and off-duty study. The professional examination is largely concerned with the manner in which you think, reason, and the intelligent, practical application of your knowledge. The ability to think, reason, and apply sound judgment to practical problems is not learned overnight, or in a concerted session of "cram" study. It is only through study and planning over a long period of time that you can develop your ability to make sound and logical decisions based upon facts.

The future outlook for appointment as Supply and Administration officers is most encouraging. It is anticipated that there will be a requirement for at least 50 new officers each year for the next five years in order to fill vacancies caused by attrition of officers in this category. Therefore, all hospital corpsmen and dental technicians who have a future interest in this program are strongly urged to make preliminary plans at an early stage in their career so that they will not be caught in the stream of poor test performance upon attaining eligibility for the program. Too much emphasis cannot be placed on the fact that planning properly, well in advance, pays rich dividends, and the man who takes advantage of the opportunities offered to him can experience a truly rewarding and satisfying career as an officer in the Medical Service Corps, U.S. Navy.

14TH ANNUAL ARMED FORCES SEMINAR ON OB-GYN AND 4TH ANNUAL ARMED FORCES CHAPTER MEETING ACOG 25-28 OCT 1965

The Navy will act as host for the subject seminar, which will be held at the U.S. Naval Hospital, Philadelphia, Pennsylvania, on the above dates.

All surgeons and residents in this specialty, on active duty are eligibile to attend.

Only a limited number of officers can be authorized

to attend the seminar on travel and per diem orders chargeable against Bureau of Medicine and Surgery funds. Eligible and interested officers who cannot be provided with travel orders to attend at Navy expense may be issued Authorization Orders by their Commanding Officers following confirmation by this Bureau that space is available. Requests should be forwarded via chain of command, in accordance with BUMED INSTRUCTION 1520.8A immediately.

—Medical Corps Training, BUMED.

In Memoriam

CAPT Thomas S. Adams MC USNR (Ret)	7 June	1965
CAPT William F. Kennedy MC USN (Ret)	6 June	1965
CAPT Roger D. Mackey MC USN (Ret)	8 June	1965
CAPT Daniel M. Shook MC USN (Ret)	19 August	1965
LCDR Ruth Mildred Barney NC USNR	10 May	1965

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